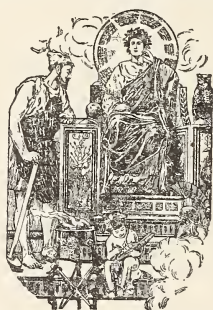


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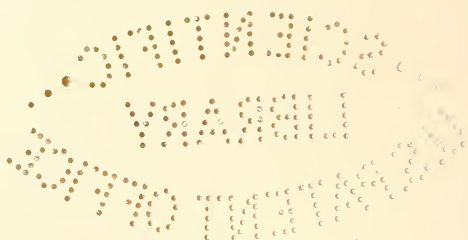
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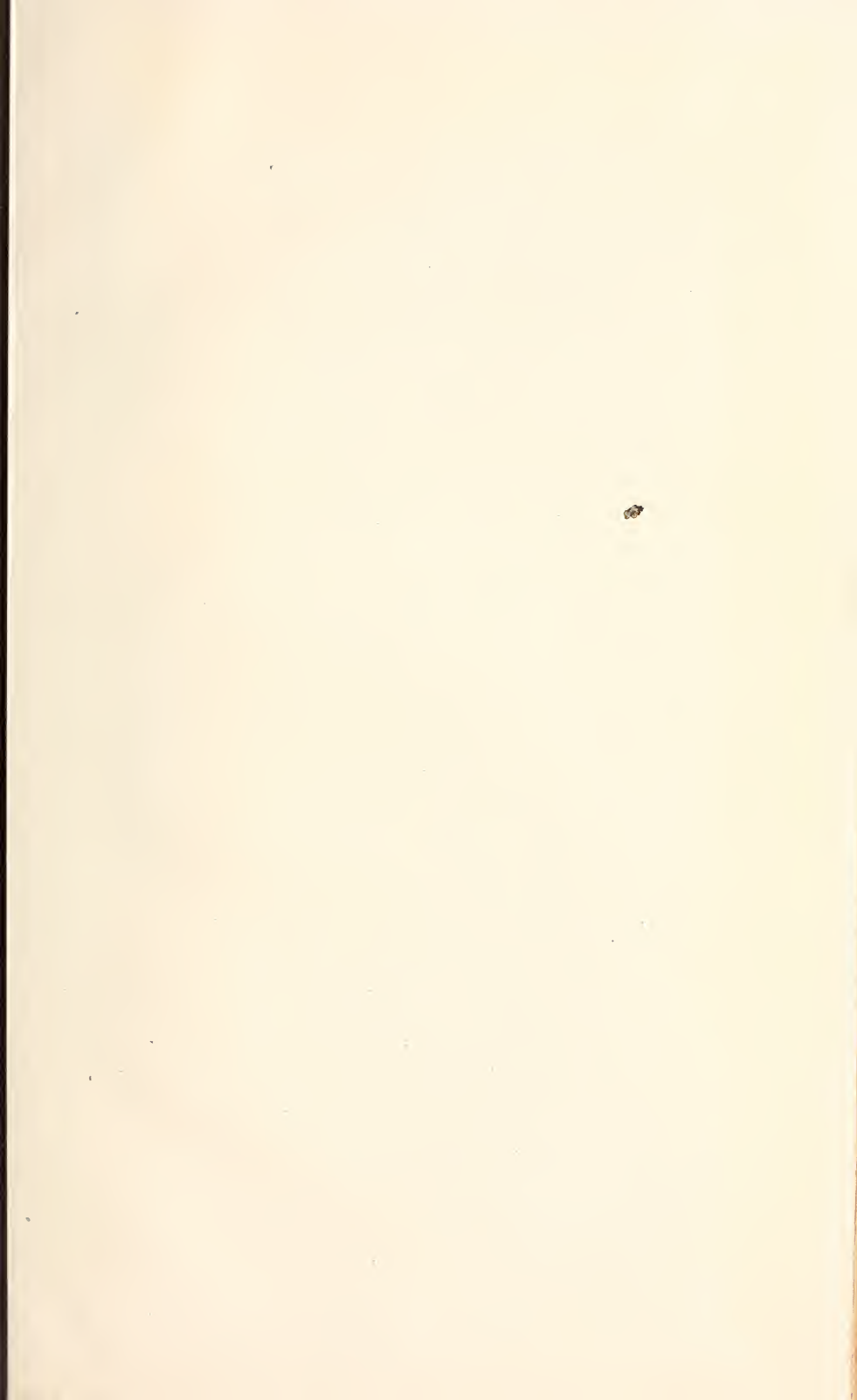
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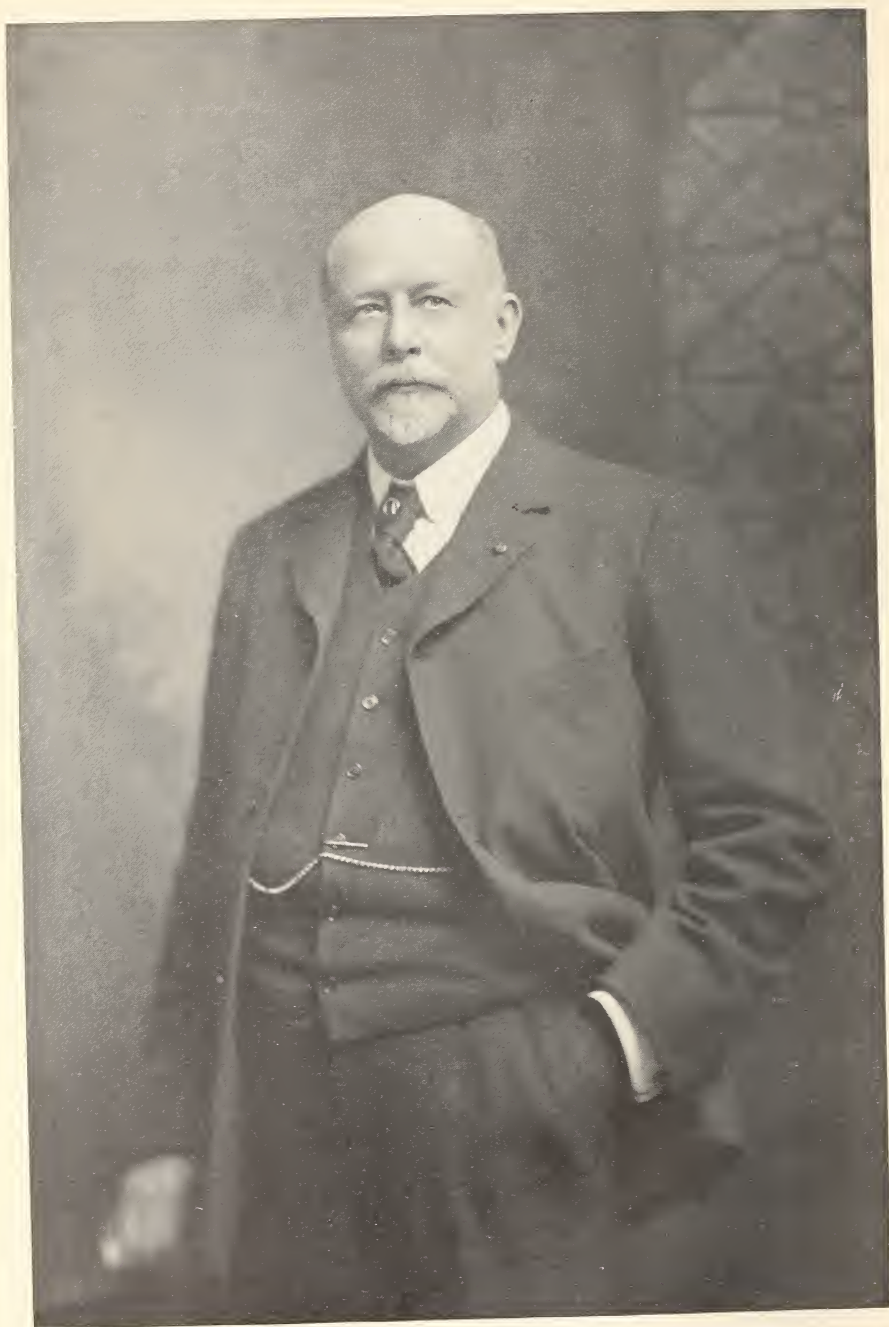


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# THE AMERICAN JOURNAL OF PHARMACY

*JANUARY, 1910*

CONCERNING THE AMERICAN MATERIA MEDICA.\*

BY JOHN URI LLOYD, PHAR.M., Cincinnati, Ohio.

## PROLOGUE.

This subject cannot be considered, even superficially, by one who comprehends, even to a degree, its outreaches, without a question as to whether, by reason of the limitation of time, that which most appeals may be reached at all. Its field touches and its substance involves the various professions and arts of medicine, botany, chemistry, pharmacy, and biology in their many and diversified phases. But scant justice can be given to most of these, for they could not be satisfactorily treated in a volume.

The course of the American materia medica has been tortuous. In an historical sense its beginnings are all-important, and must neither be evaded nor neglected by me, even though, by reason of the time consumed in its telling, that which most I crave to say be left unsaid. I do not know that any one has ever before attempted to construct an orderly sequence of its story, nor do I know that any man has ventured, in a spirit of fairness, toleration, and admiration, to say a kind word for both friend and foe involved in the mazes of past prejudice and past action, in which so innocent a theme as the American materia medica served as a text. But this issue must be met by some man, some day. The facing of it to-day is not of my choice, but it is for me a duty. I shall therefore try, in the brief hour at my command, to do what is possible to connect

\* Address delivered before the Philadelphia College of Pharmacy, November 4, 1909, being the third of a series of special lectures for 1909-10.

the past with the present. And in doing this, I shall draw not alone from what I have learned from print, but that which came from the lives of my associates, in whom I have been much blessed.

#### PART I.

CONCERNING PHILADELPHIA.—The pleasure of meeting one's friends amid such greetings as come when I visit this home of those whose work, past and present, has been in my own chosen field, is an inspiring ideal. But yet not without a degree of apprehension do I appear to-day in this institution, where it is my duty to consider discursively a subject which I shrink from attempting, even though it has taken my care and time for many decades. Well do I recall that twenty years ago I accepted in our neighboring city, New York, a like responsibility concerning a closely related subject, and at that time felt less hesitancy in attempting to discuss the "Infinities in Pharmacy," than I do now, concerning a subject on which I should, seemingly, be better informed. Let me not be misunderstood. The years of experience between then and now have been a teacher that bids me be cautious. As I now view the outreaches and intricacies of our text, the apparently more portentous one of other days is far overshadowed by that which lies within the title you have given me. Infinity, from whatever direction man's limitations meet the unknown, is incomprehensible; but no more superhuman text appears than lies within the subject awarded me to-day. This I claim to be able to demonstrate, if time and space permits me to reach the substance that rests beyond this introduction.

Need I, then, say that no one can better appreciate than do I the delicacy of the position I now occupy? Nor could any one appreciate more than do I the opportunities for error that lie in my path. Let me then be cautious, realizing, as I do, the responsibility and the complications, past and present, that I assume in touching a subject so closely connected with men's prejudices and antagonisms.

The historical surroundings of this spot take first my tenderest thought, and I crave a moment in their behalf. Am I wrong in accepting that this is the cradle in which was nourished the early American materia medica, as at that date the materia medica was known? While it is true that the Pilgrim Fathers, on the rocky coast of Massachusetts, began of necessity the investigation of a new flora in that New England land, it is also true that, creeping down the coast and across the lands and rivers intervening, the spirit

of research found here a place in which to rest, and from which to radiate. Credit for their achievements those who have achieved, be they who they may or where or when they lived, but yet concede that for a hundred years, during the burst of enthusiasm over the new land's productions, the greatest activity in the direction of my subject clustered about this spot.

In 1808 appeared, in Boston, the first Pharmacopœia of American physicians, but let us not forget that in the very building wherein I now speak, published in Philadelphia (1778), rests the only known copy of the first Pharmacopœia published authoritatively in America, under the auspices of the government of the United States. It emanated from Lancaster, almost a suburb of this city, and bore the official stamp of the embryonic nation. Could there have been a more precious book than this, issued in behalf of the struggling government? Since the publication of this epoch-marking book, a volume would be required were I even to attempt to record the titles or make a brief summary of the Philadelphia publications of world-wide celebrity on our subject.

As I think of those times and the records of the men who accomplished their mighty work in and about Philadelphia, the names of the participants that crush upon me stand second in importance to none in America. From this point the botanists Pursh and Nuttall pursued their explorations, and we all know the importance of their contributions to the study of the flora of North America. Here Dr. John Morgan became conspicuous, in that he was the first American physician to plead for the separation of the compounding of medicines from the process of medication, which, to use the words of Mr. Wilbert, he felt would be "commended in some directions, severely criticized in others."

In Philadelphia, about 1730, John Bartram established the first American botanical garden, and near here his cousin, Humphrey Marshall (1773), established the second. From the Jersey land near this point, Peter Smith began (1780) his travels down into and then through the southern country, thence back to Cincinnati, where (1812), under the title "Dispensatory," he printed the first medical book issued west of the Alleghenies. Need I call to your attention the two Bartons of one hundred years ago, and the work they accomplished, that of B. S. Barton (1798) being the first American attempt at a printed collection of the American materia medica, for that of Schoepf (1787) was issued in Germany? And



even in that foreign work, may not Philadelphia claim a full share of credit? For Schoepf was a Hessian soldier, who, on the surrender of Lord Cornwallis at a point relatively near where we now stand, travelled with pack on back from New York to Philadelphia, from which point he continued, even to Florida, searching the country throughout for *materia medica* specimens. But, as already stated, his descriptive book was, unfortunately for American records, written in a foreign tongue and printed (1787) in a foreign land. In this city the botanist preacher and pioneer Manasseh Cutler, of Massachusetts, received his doctor's degree and became a member of the celebrated Philosophical Society of Philadelphia, in the Proceedings of which (1785) appeared his "Vegetable Productions, Botanically Arranged." Here Dr. Benjamin Rush and a host of contemporary physicians served humanity's best interests, as they saw humanity's best interests under the limitations of that day. In Philadelphia was issued the rare publication, in two volumes (1828-1830), of that scholarly traveller, C. S. R. Rafinesque, whose scientific qualifications did so much to influence educational thought and action throughout the central west. I love to think of him as a professor in Transylvania University of Lexington, Kentucky, then the western centre of art, literature, and science, a colaborer with Audubon the bird painter of Louisville, Kentucky. To Philadelphia came that conspicuous searcher into America's *materia medica*, that antagonist to all forms of medication established "*by right of authority*," Samuel Thomson, to discuss with Rush, Cutler, and Barton those things pertaining to medicine in his day. Here, under the auspices of the University of Pennsylvania and the Philadelphia medical societies, such researches were made as those of Downey, on *sanguinaria* (1803), and many other theses of like importance. Indeed, notwithstanding lost opportunities, the influence of the three great institutions, the University of Pennsylvania, Jefferson Medical College, and the Philadelphia College of Pharmacy, in such as this is world wide. Wherever in this land one touches life and activity in the direction of botany, pharmacy, medicine, *materia medica*, and allied subjects there flow their united currents.

To mention even briefly the records of the men no more among us, who come to mind as I review the work done in this great city, would take more time than can be devoted to the subject concerning which I shall speak. I must not attempt to name men yet living, nor yet can I presume to pass the more recent but not less important

efforts of such men as Wood, Bache, Procter, Maisch, Trimble, Parrish, and others whose faces, no longer with us, are to me as familiar as are those of the friends now about me. Nor yet can I neglect those concerned in establishing the great chemical industries of this city, Rosengarten, Powers, Weightman, Ellis, Bullock, Crenshaw, Carter, Scattergood, Bowers, and others. These, and such as these, have been mighty factors in our work, their names are inseparable from those of whom I have been speaking and are inseparably connected with American progress.

But, my friends, these reflections or reminiscences, bred by the subject awarded me, must be broken. Let me, however, hope that what I have said may lead my hearers to realize that in addressing this audience in this building I not only fully appreciate the honor conferred upon me but comprehend that in the face of these records of the past, in which so many men unnamed were also concerned, I have good reason to be apprehensive as to whether I can do justice to that past, and yet credit myself in aiming to serve my friends as I would like to do.

EARLY CONDITIONS IN MEDICINE.—Let us now revert to conditions pertaining to the day of those involved in the introduction of the early vegetable American materia medica. In those days, primitive men (and this term need not be restricted to the aborigines) were much closer to nature than is humanity at present. In addition to nature's contact, religious thought, or perhaps we may better say theological teachings, were more nearly hand in hand with man's opinions of life's objects than they are at present. Less disposed than now were men to question (aloud) the axiom (dogma) that the universe and all contained therein was formed for the sole purpose either of serving or of pestering mankind. Diseases were likewise more apt to be likened to organic entities, partaking much of the qualities of the self-conscious devils of old that, under the auspices of an allwise Creator, delighted in torturing mankind. Seemingly, but yet as a rule without defining or perhaps comprehending the subject in these words, disease was not considered as simply a departure from the normal, but as an invading entity that must be driven out by an antagonist more powerful but yet somewhat more friendly to the suffering person. Nor is this opinion of diseases altogether a thing of the past, nor are the aforementioned conceptions of primitive men wanting in some men of our day as regards precepts and concepts. The medicine-man of the Indians

was not alone in the belief in evil spirits or in devils that afflicted people with diseases that needs be conjured and potioned out. Nor is he yet deserted.

Let us not be surprised that at that date the trend of thought of many and the personal belief of not a few was to the effect that, in nature's store-house, ready for the use of man, were locked remedial agents antagonistic to every disease which sin-laden man had contracted or inherited. It was an oft-repeated maxim, that yet lingers, that God had placed in every country remedial agents to care for diseased mankind in that country. Nor is this, as already indicated, foreign to the belief of some to-day.

Let it not be accepted, however, that all men at that date were imbued with or even tintured by this theological inheritance or professional conception. On the contrary, many talented investigators of what was known then as *materia medica* looked upon disease, as well as upon remedial agents, in quite a different manner. They believed, it is true, that nature possessed secret wealths that could be utilized by man for man's benefit (often through torture of the flesh), but which, yet, were no more *created* for man than that man was created for the purpose of being attacked by diseases or persecuted by evil spirits.

Thus came into play in the incipency of the early American *materia medica* a blending of the intensely religious, the professionally dogmatic, and the hopefully scientific, as well as the ever-present commercially ambitious, all seeking alike the secrets that reposed in the natural products of the new world.

And yet another vital factor in the primitive development of the American *materia medica* must not be overlooked. In those days, authoritative remedial agents of European pharmacy were difficult to obtain. This necessitated the discovery of agents that would parallel the action of the old-time remedies. Emetics, cathartics, vesicants, anthelmintics, and such were seemingly as necessary to man's existence as food. The pioneers were versed in domestic medicine, and many were familiar with European works on the subject. They felt compelled to seek for substances possessed of qualities similar to those commended by such authors as Lewis, Culpepper, and Quincy.<sup>1</sup> Nor was this all. The marvellous stories

<sup>1</sup> Selecting therefrom too often the substances that produced systemic shock. Let it not be forgotten that the European herbalists attempted to utilize about every plant that grew.



told by the new world *promoters* concerning the fabulous wealth of soil and flora of the new-found land, the almost superhuman qualities imputed to some of the products by the advertising real-estate promulgators, fired the European mind and prepared settlers for almost any *materia medica* surprise. Witness, even in the days so near us as those immediately preceding the Revolution, the exaggerations concerning the Kentucky land, whose story was so graphically told in John Filson's "History of Kentucky." Witness also the marvellous record of cinchona (*Jesuit bark*) from South America, and of *sassafras* from "the Floridas." Think of the sensational introduction into Europe of tobacco, and the new foods, Indian corn and the potato. Comprehending all this and such as this, one may be in a position to realize the speculative importance to a half-clothed, suffering, needy, transplanted people, on the fringe of an undeveloped continent, of the blessings that might lie within an unknown flora, boundless in extent.

That was a day of heroics in therapy, and under the influence of tradition and environment substances most likely to gain a receptive hearing were such as strongly appealed to the senses by reason of their aromatic, emetic, cathartic, or other energetic qualities. *Sassafras*, *serpentaria*, *senega*, *podophyllum*, *spigelia*, and such, from North America, *ipecac* from the eastern coast of South America, cinchona and jalap from the land of the Incas, and such substances as *hydrastis* and *sanguinaria*, used by the Indians as pigments by reason of the fact that they both possessed bright colors and their juices were distasteful to pestering insects, may thus be cited.

With these thoughts in mind, let us now refer to Barton's "Collections," published in Philadelphia in 1798. Note the discreet sentence in the *Introduction*, indicating the fact that Dr. Barton comprehended the delicacy of his position as concerns both the people and the profession, for in those days, as already indicated, the people were deeply interested in *materia medica* subjects and were preparing to rebel against transplanted, mediæval European processes employed by the regular profession. This is apprehended by Barton, as follows:

The readers of these "Collections" (for everything that is written and published solicits some readers) will form different opinions about my medical faith. Some of them will think I have too much; and others, that I have not enough.

Comes then the question as to what should be a part of the materia medica, concerning which the doctor asks a question as pertinent now as it was then, to wit,

How are we to know what plants are most proper for the purposes of medicine, until we shall have examined the properties of a great body of vegetables?

Then comes a plea for toleration by his professional brethren :

I wish to turn the attention of our physicians to an investigation of the properties of their native productions. When it is considered how little has hitherto been done in this way, every attempt (mine is an humble one) should be candidly received.

Next, in a cautious criticism, he applies himself directly to physicians, informing them that little had been done in the direction of the investigation of the American materia medica.

Skim now the substances suggested by Barton as being worthy of examination and their sources. Note that he credits alike Indian, pioneer, traveller, botanist, farmer, attorney, and statesman, mentioning Thomas Jefferson, then President of the United States, as commending a treatment to overcome a disease then prevalent in Virginia. But seldom does he credit a member of the medical profession as having done anything whatever ! Note more specifically the importance given to energetic drugs, both those experimented with and those that were promising by reason of their relationship, botanically, to poisonous remedies in use. A few are kindly in their action, as, for example, *cornus florida*, *boneset*, and *uva ursi*, the *majority*, however, being possessed either of exceedingly disagreeable qualities or of very energetic natures, such as emetics, cathartics, anthelmintics, vesicants, or bitter tonics. Thus Barton indicates his self-satisfaction with, or at least his subjection to the heroic theory. In a lengthy article on *phytolacca* he commends its investigation because " it is certainly a plant of great activity." The fact that *Rhus radicans* produces such a terrible eruption as is the case with some people is most clearly stated by the doctor, after which he indicates where and how the decoction or the plant in substance can be used *safely*, with benefit in disease. As previously indicated, the trend of thought in those days in the medical profession was to discover substances that in action would parallel European energetic drugs. Senega is thus hopefully mentioned by Barton, as follows :

My ingenious pupil, Dr. Thomas Walmsley, has lately communicated to me an additional instance of the *salivating* power of this active vegetable.

He questions the *power* of *datura* in overcoming so virulent a disease as tetanus, as follows:

I fear that our vegetable, though by no means a *feeble* one, will be found unequal to the cure of this terrible disease.

In this sentence he unconsciously voices the transplanted idea of mediæval medicine, to the effect that *severe diseases* require *heroic treatment*.<sup>2</sup>

Among emetics, sanguinaria is conspicuous. The doctor believes by reason of the *acid nature* of the *Indian turnip*, that it deserves careful investigation concerning its *promising therapeutical qualities*.

Among stimulants, the poisonous side of plants is the subject of hopefulness. For example:

I have no hesitation in referring to a number of poisonous vegetables, with the properties of which we are not so well acquainted as we ought to be. Such are the *Datura Stramonium*, or Jamestown weed, the *Cicuta maculata*, &c.

Concerning *Cicuta venenosa*, a fearful poison which kills as he states, "without inducing pain or convulsion," he adds that perhaps it is "the plant with which some of our Indians destroy themselves." He adds that it should be used with great care, concluding as follows:

I have given the powder of this plant internally in a case of fever, and have thus, at least, ascertained that it may be used with safety.

Happily, among stimulants are included a few innocuous plants, gaultheria, sassafras, spicewood, ginseng, and eryngium.

Not less energetic are the *topical stimulants*, among which, in addition to the acid crowfoot, the cathartic butternut and a few other items are included as follows:

To this head of topical stimulants, I may refer several species of the genus *Rhus*, or *Sumac*; particularly the *Rhus radicans*, or poison vine; the *Rhus vernix*, or Vernice tree; and the *Rhus toxicodendron*, or poison oak.

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<sup>2</sup> Let it not be forgotten that the European herbalists were not poisoners. They perhaps erred in the direction of credence in innocuous plants of no established value.

But enough for our purpose. Throughout the "Collection" we note, as has been stated, that remedial agents thought of as members of the American materia medica, and used both by the "empiricists" and the profession, partake of energetic natures or of strikingly disagreeable qualities.

Consider now the significance of what we have before us in a general application to the American materia medica. Dr. Barton was a cultured, kindly gentleman, and one of the foremost thinkers of his time. He was conspicuous as a botanist and was therefore acquainted with America's flora, being likewise hand in hand with men versed in therapy and chemistry. He was an educated man, tolerant of error and mistakes, kindly disposed towards empiricists and those engaged in domestic medication, a listener to men with information or experience records to impart, whether or not they were qualified in outside lines. He was in touch with the pioneer and the Indian, as well as adventurers who travelled in outside places, and he came into close communication with primitive men and with nature. Notwithstanding all this, we find that the "Materia Medica Americana" of Dr. Barton, known as Barton's "Collection," breathes in its every page the touch that seems to have been inherited from the spirit of mediæval European times, in which kindness to the sick and charity for the afflicted were too often exceptional. Confronting evil spirits, although not designated as devils, seemingly needed to be expelled by energetic, harsh forms of medication.

## PART II.

BEGINNING OF A REVOLUTION.—Comes now the spirit of unrest, that, cradled during preceding years, about this date took possession of the people. There were questionings and criticisms of "authority" in medicine, that success in the great American Rebellion had perhaps made possible. Inherited methods from abroad, political or religious, were no longer accepted merely by right of inheritance or of official authority. Rebellion in politics and by arms bred rebellion in expanding thought. Inherited medicines and authoritative medication as practiced by physicians became a storm-centre of attack. European text-books, European remedies, European processes, surgical, therapeutical, pharmaceutical, came by a great part of the people to be viewed with suspicion. The rebellious populace, often illiterate and destitute of scientific education, presumed to criticize the methods as well as the practice of the medical profes-



sion. The terms *bleeders*, *blisterers*, and "*fashionable doctors*" were hurled against physicians of regular professional education. Empiricists, believing in domestic medication and the possibilities thereof, in contradistinction to regular medication, issued pamphlets, wrote communications to the papers, travelled about the country giving lectures and otherwise decrying the evils of the processes inherited from Europe and paralleled in America. "Better that our loved ones should be permitted to die in peace than by the torturer's hand." That cry became a battle cry.

SAMUEL THOMSON THE BOTANIC CRUSADER.—Just then came Samuel Thomson as the most pronounced of all the agitators. Dogmatic, aggressive, unflinchingly persistent, closely did he touch the people and irresistibly did he appeal to them. Throughout the country his followers and himself travelled, introducing the new "American" practice and arraigning those whom they called "*fashionable doctors*." The evils of bleeding, the depleting effects of violent cathartics, of blistering and of salivating were most forcibly and excoriatingly set forth. Nor could they well be exaggerated. Thomsonianism. (better had it been *Thomsonism*) became a household word. Empiricism as concerns medication became the fashion with thousands. Household remedies now grew in importance, whilst home-prepared remedies were most extravagantly praised. In it all the educated physician was berated and abused without stint and without mercy. The good in his work was forgotten, the bad (and there was much bad) was never overlooked. Seizing upon the nature of the heroic remedies that were favorites Thomson and his people raised the battle cry against such methods and against such remedies. For reasons that are apparent as we look back into those days they instituted a crusade that finally succeeded. Notwithstanding the illiteracy of so many of its advocates, the rebellion against the regular profession spread like a prairie fire. The fame of Thomson and the Thomsonian remedies became established in the homes of the people throughout America, from Massachusetts to the Carolinas.

(To be concluded in February number.)

THE PHARMACOPŒIAL TESTS FOR AMMONIUM  
BENZOATE.\*

BY ATHERTON SEIDELL AND GEORGE A. MENGE,

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The United States Pharmacopœial description of this salt contains, in addition to the qualitative tests for ammonia, benzoic acid, and certain common impurities, only two tests which might be expected to indicate the degree of purity of the sample. These are the melting or, rather, decomposition point, and the reaction towards blue litmus paper. The following experiments show that neither of these tests is of any value in determining the purity of a given sample of the salt. The experiments we have made also show that the distillation method for ammonia determination is readily applicable to the analysis of ammonium benzoate samples and a simple adaptation of this process is therefore suggested as a quantitative method for this and similar Pharmacopœial ammonium compounds.

*Analysis of Ammonium Benzoate by Distillation of the Ammonia.*—The distillation method modified to the simplest conditions was found to give entirely trustworthy results. The details which were followed in the determinations reported herewith are as follows: The distillation flask was an ordinary Erlenmeyer Jena glass flask of about 350 c.c. capacity, through the stopper of which passed a plain glass tube which was bent to form an inverted U, the longer arm of which ended below the surface of the standard acid contained in the receiving flask, which was placed in an evaporating dish containing cold water. The connections which would have been required for a condenser were therefore eliminated, and the rapidity of the distillation was not appreciably affected. Tenth normal solutions were used in all cases. A convenient amount of the sample for a determination is 0.5 Gm. for which 50 c.c. of 0.1 N  $\text{H}_2\text{SO}_4$  are to be used in the receiving flask and 50 c.c. of 0.1 N caustic alkali and about 150 c.c. of water in the distilling flask. About 150 c.c. of liquid are distilled over, and

\* Presented in abstract at the meeting of the Pharmaceutical Division of the American Chemical Society, December, 1909.

the excess of acid remaining in the receiving flask titrated, after cooling, with standard ammonia solution, using cochineal as the indicator. The free alkali remaining in the distilling flask may also be determined by titration, with 0.1 N  $\text{H}_2\text{SO}_4$  using phenolphthalein, but calculations made from this titration are subject to the error arising from the alkali dissolved from the glass of the distilling flask and also from inaccuracies of the indicator. With

TABLE I.

ANALYTICAL RESULTS OBTAINED UPON AMMONIUM BENZOATE SAMPLES BY THE DISTILLATION METHOD.

(50 c.c. 0.1 N NaOH and 50 c.c. 0.1 N  $\text{H}_2\text{SO}_4$  used respectively in the distilling and receiving flasks for each determination.)

Sample		Distilling flask			Receiving flask			Per cent. $\text{C}_6\text{H}_5\text{COONH}_4$ found
		C.c. 0.1 N $\text{H}_2\text{SO}_4$ for excess NaOH	C.c. 0.1 N NaOH equivalent to $\text{C}_6\text{H}_5\text{COO}$	Calc. Gm. free $\text{C}_6\text{H}_5\text{COOH}$	C.c. 0.1 N $\text{NH}_4\text{OH}$ for excess $\text{H}_2\text{SO}_4$	C.c. 0.1 N $\text{H}_2\text{SO}_4$ equivalent to $\text{NH}_3$	Calc. Gm. $\text{C}_6\text{H}_5\text{COONH}_4$	
No. 220.....	0.5	14.0	36.0	.006	14.5	35.5	.494	98.8
No. 220.....	0.5	13.9	36.1	.005	14.35	35.65	.496	99.2
No. 222.....	0.5	13.85	36.15	.003	14.1	35.9	.499	99.9
No. 223.....	0.5	13.75	36.25	.004	14.1	35.9	.499	99.9
No. 224.....	0.5	13.9	36.1	.003	14.15	35.85	.498	99.7
No. 220 recryst. (a) ..	0.5	14.0	36.0	.003	14.3	35.7	.496	99.2
No. 220 recryst. (b) ..	0.564	9.4	40.6	.003	9.6	40.4	.498	99.6
No. 220 recryst. (c) ..	0.4323	18.65	31.35	.0067	19.2	30.8	.428	99.1
No. 220 recryst. (c <sub>1</sub> ) ..	0.4365	13.3	31.7	.0232	20.2	29.8	.415	95.0
No. 220 recryst. (c <sub>2</sub> ) ..	0.4838	14.6	35.4	.0330	17.3	32.7	.455	94.0
No. 220 recryst. (c <sub>3</sub> ) ..	0.4186	19.35	30.65	.0494	23.4	26.6	.370	88.4
No. 220 recryst. (c <sub>4</sub> ) ..	0.2466	31.1	18.9	.1062	39.8	10.2	.142	57.5

In the above table the designations "recrystallized (c), (c<sub>1</sub>), (c<sub>2</sub>)," etc., refer to the same sample of purified ammonium benzoate, which was dried in a Hempel desiccator containing  $\text{H}_2\text{SO}_4$  and at about 50 mm. Hg pressure for successive periods of time. These periods were respectively about 1, 2, 5, and 8 days.

samples containing large amounts of free benzoic acid, however, this latter titration serves as a useful check upon the results calculated from the ammonia determination. The character of the results which may be obtained by the method as above outlined are given in Table I.

In connection with the distillation method, it should be mentioned that on account of the low percentage of ammonia ( $\text{NH}_3 =$



12.24 per cent.) in the compound the multiplication of the error in calculating to benzoate is considerable, and therefore the accuracy of the method is probably within only about 0.5 per cent. of the amount of the salt present. It is interesting to note that of the four commercial samples analyzed they all gave results above 99 per cent. The Pharmacopœial purity rubric of 98 per cent. for this compound might, therefore, be raised to 99 per cent. without requiring a change in the present market conditions of this product.

*The Formaldehyde Method for the Analysis of Ammonium Benzoate.*—This method, which depends upon the formation of hexamethylenetetramine and simultaneous liberation of the acid of any ammonium salt when an excess of a neutral solution of formaldehyde is added to it, was suggested by Schiff<sup>1</sup> and subsequently by Ronchèse.<sup>2</sup> Dr. B. Herstein, of the Drug Laboratory, Bureau of Chemistry, Department of Agriculture, recently tested this method (private communication) upon a large number of ammonium salts, including the sulphate, nitrate, phosphate, oxalate, citrate, molybdate, halogen salts, etc., and found that entirely satisfactory results were obtained.

The determination may be very conveniently made as follows: about 5 c.c. of the ordinary 40 per cent. formaldehyde is just neutralized in an Erlenmeyer flask with dilute alkali solution, using phenolphthalein as indicator, an aliquot portion of the ammonium salt solution corresponding to 0.5 Gm. is then added, and the liberated acid titrated to the first appearance of the pink color of the phenolphthalein, with 0.1 N NaOH; the solution is then heated just to the boiling point and a further amount of alkali added to the reappearance of the faint pink color. Our experiments showed that satisfactory results were not obtained when less than 3.0 c.c. or more than 10 c.c. of 40 per cent. formaldehyde were used per 0.5 Gm. of ammonium benzoate. The analytical results are given in the following Table II.

These results confirm the general conclusion that the formaldehyde method is very satisfactory for the determination of the acid radicle, and should, no doubt, be adopted as the quantitative method for most of the ammonium compounds of the Pharmacopœia. It happens, however, in the present case that, since the most common impurity of ammonium benzoate is free benzoic acid resulting from

<sup>1</sup> Liebig's Annalen, 319, 75, 1901; Chem. Ztg., 27, 14, 1903.

<sup>2</sup> Jour. pharm. et chim. (6), 25, 611, 1906.

the gradual loss of ammonia, the inferiority of a given sample due to this cause is not detected as readily by the formaldehyde as by the distillation method of analysis. This fact is very forcibly illustrated by the titration of the mixture of ammonium benzoate and benzoic acid shown above. In this case, although there was present 20 per cent. of free benzoic acid, there was obtained a difference of only 1.15 c.c. (37.1-35.95) of 0.1 N NaOH from the amount theoretically required for pure ammonium benzoate. Thus, by the formaldehyde method each 0.115 c.c. of 0.1 N NaOH, when 0.5 Gm samples are employed, corresponds to 2.0 per cent. of free benzoic acid. By referring to Table I it will be found by calculation that, on the basis of the ammonia determination, the presence of 2.0

TABLE II.

ANALYTICAL RESULTS UPON AMMONIUM BENZOATE SAMPLES OBTAINED BY THE FORMALDEHYDE METHOD.

Sample No.	Gms. used	C.c. neutralized 40 per cent. formaldehyde	C.c. 0.1 N NaOH required		Calc. per cent. $C_6H_5COONH_4$
			Before boiling	After boiling	
222	0.25	1.0	17.1 ?	17.65	98.2
222	0.25	3.0	17.85	17.95	99.9
224	0.50	6.0	35.45	35.95	100.0
223	0.50	8.0	35.45	35.95	100.0
220	0.50	10.0	35.55	36.05	100.3
Mixture *	0.50	6.0	36.7	37.1	103.2

\* Mixture = 0.4 Gm. No. 224 + 0.1 Gm.  $C_6H_5COOH$ , i.e., 20 per cent.  $C_6H_5COOH$ .

per cent. free benzoic acid is indicated by a difference of 0.74 c.c. of 0.1 N  $H_2SO_4$  from the amount theoretically required for pure ammonium benzoate. The explanation of this advantage of the distillation over the formaldehyde method in the case of ammonium benzoate is that a given difference between the composition of two samples is a larger percentage of the ammonia than of the benzoic acid present, and therefore shows itself in nearly the ratio of the amounts of these two constituents in the compound.

*Stability of Ammonium Benzoate in the Air.*—Although it is stated in the Pharmacopœia that the salt gradually loses ammonia when exposed to the air, the observations which we have made indicate that such a decomposition is very slight and need not be feared with the use of ordinary precautions for protecting the sample.

Several grams of ammonium benzoate, through which a slow current of air was drawn for eighteen hours, lost an amount of ammonia corresponding to about 2 per cent. of ammonium benzoate, and it appeared that the alteration had all taken place at the point where the current of air first met the sample. Of five samples of ammonium benzoate kept in an ordinary desiccator, over  $\text{H}_2\text{SO}_4$  for two and one-half months, four lost ammonia corresponding to about 5-8 per cent. of ammonium benzoate. The fifth, however, lost an amount corresponding to 20.7 per cent. Under diminished pressure, as might be expected, the loss of ammonia is very rapid, as will be seen by reference to the last four analyses given in Table I, and to the experiment described in connection with the melting-point determinations.

*The Pharmacopœial Litmus Paper Test.*—On applying this test to a number of samples containing varying per cent's of benzoic acid, it was found that even as high as 8 per cent. of the latter produced no distinct change in blue litmus paper; with samples containing 12 per cent. benzoic acid, however, the change could be detected. It is therefore apparent that the litmus paper test is valueless as an indication of the partial deterioration of ammonium benzoate within the limit stated.

*Melting or Decomposition Point of Ammonium Benzoate.*—The specifications under ammonium benzoate, in the Pharmacopœia, contain the following statement: "The salt fuses at  $193^\circ$  to  $194^\circ$  C. ( $379.4^\circ$  to  $381.2^\circ$  F.) with decomposition . . ." Considered in connection with the purity rubric of 98 per cent., this statement would doubtless be generally construed to mean that if a sample of ammonium benzoate fuses with decomposition at  $193^\circ$  to  $194^\circ$  C., it may be considered to be 98 per cent. pure or very nearly so. Upon this assumption and in connection with an investigation now being conducted in this laboratory upon the melting points of Pharmacopœial compounds, the decomposition point of four samples of ammonium benzoate had been determined, with results that were practically concordant for the different samples and with the U.S.P. requirement, thereby indicating a purity of at least 98 per cent., which subsequent analyses confirmed. The analytical data for the different samples, however, showed a variation as great as 1 per cent., with no corresponding variation of the decomposition point. Another sample which had been kept in a vacuum desiccator for a short time and was found upon analysis to contain only 94

per cent. of ammonium benzoate, also showed a decomposition point practically identical with that of the pure material. These results led us to a more extended and systematic investigation of the effect of the presence of benzoic acid upon the decomposition point of ammonium benzoate.

Since benzoic acid is the impurity which results when ammonium benzoate is partially decomposed, we approached the problem from the two extremes of ammonium benzoate and benzoic acid, obtaining two series of samples which gradually approached each other in composition. The first series was obtained by subjecting pure ammonium benzoate to continual desiccation in the presence of sulphuric acid in a Hempel desiccator under diminished pressure (about 50 mm.), portions being removed at irregular intervals for analytical and melting-point determinations. In this way we obtained six samples, varying in composition from 98.6 per cent. to 57.5 per cent. ammonium benzoate. The last sample (57.5 per cent.) exhausted the supply of material we started with in that experiment. The second series was obtained by mechanically mixing benzoic acid and ammonium benzoate in proportions varying from 50 per cent. each at the one extreme to pure benzoic acid at the other, six samples being prepared in this way.

The melting or decomposition points determined for the different samples of both series, together with the duration of desiccation required to produce the varying degrees of decomposition indicated in the first series, will be found in the following table. The samples of the first series have been designated by Roman numerals and those of the second by letters. The method used for determining the melting points is one recently adopted in this laboratory, according to which the material, within certain limits, is heated at a definite rate ( $3^{\circ}$  per minute within  $20^{\circ}$  or  $25^{\circ}$  of the melting point). A standard thermometer was used and the observed reading was corrected for emergent stem.

It would seem to require only casual consideration of the tabulated data to lead to the very definite conclusion that the decomposition point of ammonium benzoate is quite useless as a test of purity—at least, in the presence of benzoic acid, even to the extent of nearly 50 per cent.—and that, therefore, the statement previously quoted from the Pharmacopœia relative thereto should either be modified so as to insure against misinterpretation or should be omitted. The melting-point results of the mixtures shown in



Table III are perhaps more clearly exhibited by the following graphic representation. The lower curve shows the temperatures at which the various mixtures began to melt—the beginning of the melting being understood as that point at which the sample collapses or sinks down in the capillary, or that point at which the first definite trace of liquid can be detected. The upper curve repre-

TABLE III.

MELTING POINTS OF MIXTURES OF AMMONIUM BENZOATE AND BENZOIC ACID

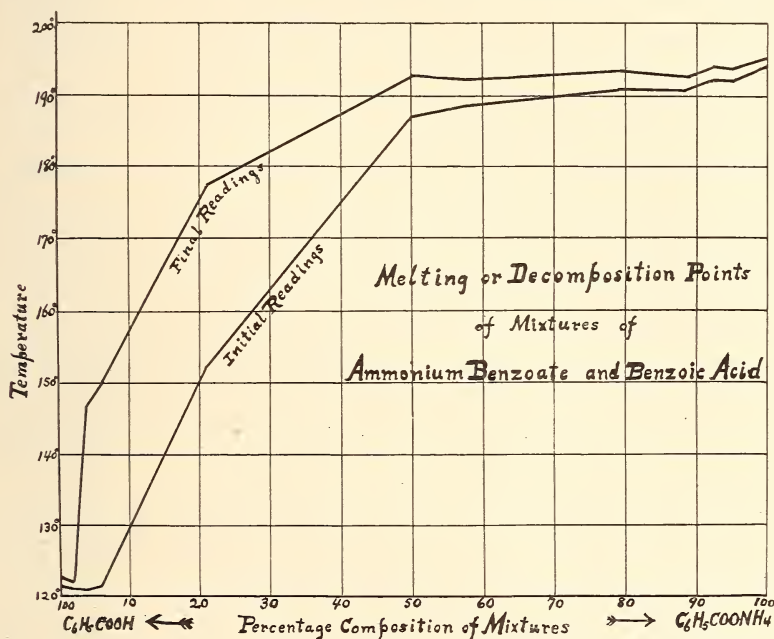
Sample	Per cent. composition		Melting or decomposition point (cor.)	Remarks
	C <sub>6</sub> H <sub>5</sub> COONH <sub>4</sub>	C <sub>6</sub> H <sub>5</sub> COOH		
I	99.2	Trace	192.5° to 194.3°	Vigorous effervescence.
I <sub>a</sub>	99.2	Trace	188.2° to 189.2°	Effervescence after 5 to 7 min.
II	99.6	Trace	193.° to 194.3°	Vigorous effervescence.
III	99.9	Trace	193.1° to 194.8°	Vigorous effervescence.
IV	99.7	Trace	193.8° to 194.8°	Vigorous effervescence.
V*	98.6	1.2	193.1° to 194.3°	Vigorous effervescence.
VI*	94.	6.4	191.7° to 193.5°	Vigorous effervescence.
VII*	92.1	8±	192.6° to 194.°	Vigorous effervescence.
VIII*	88.4	11.8	190.4° to 192.4°	Effervescence.
IX*	79.29	20.5±	190.7° to 193.3°	Slight melting and effervescence.
X*	57.5	43.	188.6° to 192.2°	Last trace effervesces slightly.
A	49.83	50.17	187.1° to 192.7°	Slight effervescence finally.
A <sub>1</sub>	49.83	50.17	183.9° to 190.2°	Heated very slowly from 175.
B	21.	79.	152.° to 177.7°	Definite sign at 120–121 but no liquid until 152; no effervescence.
C	5.73	94.27	121.3° to 122.3° to 148.9°	Most melts 121–2; no effervescence.
C	5.73	94.27	121.3° to 131.5° to 149.°	C remelted after cooling.
D	3.85	96.15	120.8° to 121.3° to 146.9°	Behavior similar to C.
E	2.2	97.8	121.3° to 121.8°	Melts without decomposition.
F	....	100.0	121.4° to 122.4°	Melts without decomposition.

\* Samples VII and IX represent degree of decomposition of two samples of ammonium benzoate as a result of standing in an ordinary desiccator over sulphuric acid for about 2½ months. Samples V, VI, VIII, and X were obtained by subjecting a sample of pure ammonium benzoate to vacuum desiccation (about 50 mm. Hg), in the presence of sulphuric acid for 6, 42, 112, and 184 hours respectively.

sents the final reading—not necessarily the point of complete liquefaction, for in all cases where 80 per cent. or more ammonium benzoate was present the effervescence was sufficiently vigorous to drive the material up the tube and in those cases the final reading represents the point of vigorous effervescence. The distance between

the two curves at any point represents the range over which the sample was melting or decomposing (heating at the rate of  $3^{\circ}$  per minute).

The curves show clearly that the variation in melting point or decomposing point between a sample of pure ammonium benzoate and a sample containing 50 per cent. of benzoic acid is barely significant. They also offer a striking commentary upon the general conception of the melting points of binary mixtures compared to the



melting point of either constituent in pure form. The almost horizontal course of the curves from 100 per cent. to 50 per cent. ammonium benzoate and the very sharp rise at 94 per cent. to 96 per cent. benzoic acid are very striking. The nature of the curves would doubtless be more or less modified by further experimentation, and perhaps by more refined methods, but for the principal purpose of this work we believe they serve just as well as they stand,—to illustrate the unavailability of the decomposition point as a test of purity.

A further indication that the decomposition point is an unreliable test for purity consists in the fact that widely varying results may



be obtained by varying the rate of heating or by holding the temperature at a given point; for example, in one experiment we were able to cause a sample of pure ammonium benzoate to decompose at  $185^{\circ}$  by holding the temperature at that point for a few minutes ( $I_a$  and  $A_1$ , Table III). The same thing has been shown to be true of other compounds which decompose on heating.

Further investigation of binary mixtures containing ammonium benzoate, also containing other compounds which decompose, will probably be conducted in this laboratory in connection with the investigation of melting points of Pharmacopœial compounds previously referred to in this article.

*Conclusions.*—1. The results of the simplified distillation method are shown to be sufficiently accurate for the quantitative analysis of Pharmacopœial ammonium benzoate samples. This method is better adapted to the quantitative examination of ammonium benzoate than the formaldehyde method. The latter, however, is no doubt preferable in the case of most of the remaining ammonium compounds of the Pharmacopœia.

2. The melting point or rather decomposition point of ammonium benzoate is shown to be valueless as a test for the purity of this compound. It is probable, although it cannot be stated with certainty, that with all other Pharmacopœial products having a melting point accompanied by decomposition this test for purity is, as in the case of ammonium benzoate, useless.

3. The litmus paper test is shown to be inadequate for the detection of free benzoic acid present in amounts as great as approximately 10 per cent., and is therefore misleading.

4. The Pharmacopœial description and tests for ammonium benzoate should be modified by the elimination of the litmus paper and melting-point tests, or such a qualification of the latter that will show its inapplicability as a test for purity. The quantitative estimation of the ammonia by distillation may be briefly described according to the present style of the Pharmacopœia as follows:

The ammonia from a weighed portion of about 0.5 Gm. of the sample, dissolved in  $H_2O$ , made alkaline with 50 c.c. of 0.1 N NaOH, is distilled into 50 c.c. of 0.1 N  $H_2SO_4$  and the excess of the latter remaining after the distillation should require not more than 14.1 c.c. of 0.1 N  $NH_4OH$ , indicator cochineal.

## SOME SUGGESTED STANDARDS AND CHANGES FOR THE U.S.P.

BY CHARLES H. LAWALL.

The following notes have been collected during a period of several years and embody observations made from a practical application of the various tests and requirements of the U. S. Pharmacopœia in examining a large number of substances. Some of them are not entirely new, but a number of the suggestions have not appeared in pharmaceutical literature, to the author's knowledge. They are submitted as being along the lines of constructive criticism.

*Acidum Sulphurosum.*—As this preparation is very prone to deteriorate rapidly, there should be a statement to the effect that the concentrated product should be assayed and diluted at the time of dispensing. This is preferable to the present official method of assay and immediate dilution and would eliminate the necessity of advising its frequent assay as given in the text.

*Alcohol.*—The present official method of testing for wood alcohol has been alleged to be unreliable. It would be advantageous, therefore, to substitute some authoritative method like the Riche-Bardy process of the A.A.O.A.C., as given in U. S. Department of Agriculture Bulletin No. 107.

*Alumen Exsiccatum.*—As recently stated by other investigators the rubric should be brought into complete accord with practical requirements. If strictly interpreted it does not allow even a trace of moisture. This is impracticable. A limit of moisture should be given (not more than 2 or 3 per cent.) and a method for its estimation should be included.

*Amylum.*—Some commercial varieties of corn-starch contain appreciable amounts of nitrous acid or nitrites, which might occasion difficulty in its use as an indicator. A test for the presence of nitrous acid or nitrites by the Griess-Ilosvay method should be given.

A method for the estimation of the 95 per cent. of hydrolizable carbohydrates should also be included if this requirement is retained.

*Aqua Hamamelidis.*—A test for the presence of methyl alcohol should be given among the requirements for this article, as it is frequently reported as containing this substance instead of ethyl alcohol.

*Aqua Hydrogenii Dioxid.*—A test for the presence of acetanilid should be given. The following is suggested:

If 100 c.c. of solution of hydrogen dioxide be shaken in a separatory funnel with chloroform, and the chloroformic layer drawn off and evaporated spontaneously to dryness, the residue, when taken up with solution of potassium hydroxide, 1 in 4, and heated in a test-tube with a few drops of chloroform, should not evolve the disagreeable odor of phenylisocyanide (isonitrile).

*Elixir Ferri, Quininæ et Strychninæ Phosphatum.*—A method of quantitatively estimating strychnine in the presence of quinine is needed. In case of an error, where the quantity of strychnine might be in dangerous excess, there is no method of ascertaining whether the proper ratio of the two alkaloids has been used.

*Ferri Sulphas Exsiccatus.*—A purity rubric should state the amount of allowable moisture, and a method for its estimation should be given.

*Fluidextractum Zingiberis.*—A test for the presence of capsicum is advisable. The following is suggested:

Five c.c. of fluidextract of ginger are to be heated in a shallow evaporating dish with 10 c.c. of half normal alcoholic potassium hydroxide solution and the liquid allowed to evaporate to dryness on the water-bath. The residue is then dissolved in 50 c.c. of water and transferred to a separatory funnel, 20 c.c. of ether are added, and the liquids are thoroughly mixed by agitation. If the ethereal solution be drawn off and allowed to evaporate spontaneously upon a watch glass the residue left by its evaporation should have a warm, camphoraceous taste, but no sharp pungency should be observed when the tip of the tongue is applied to the residue.

*Glyceritum Ferri, Quininæ et Strychninæ Phosphatum.*—As previously noted under elixir ferri, quininæ et strychninæ phosphatum.

*Hydrargyrum cum Creta.*—A purity rubric should be given, together with a process for estimating the amount of metallic mercury present in this preparation.

*Linimentum Camphoræ.*—A rubric should be included for the required percentage of camphor.

An identification test for the presence of cottonseed oil should be given, preferably Halpen's test, which gives very good results in practice.

A quantitative test for the amount of camphor should also be included. Either of the methods proposed by Prof. E. Fullerton

Cook in the N.J.P.A. Proceedings for 1905, will be found to be satisfactory. The following, taken from that source, is suggested:

A convenient quantity of camphor liniment, approximating 10 Gm., should lose not less than 20 per cent. nor more than 22 per cent. of its weight when heated upon the water-bath during twenty-four hours and weighed occasionally until a practically constant weight is reached. The following might also be included:

When observed in a 200 mm. tube in a polariscope having a sugar scale, the number of degrees observed divided by the factor 2.925 will give the percentage of camphor in the preparation.

Or this: The specific rotatory power of the sample divided by 4.694 equals the percentage of camphor in the sample.

*Linimentum Chloroformi*.—This preparation is one that is frequently found of deficient quality, particularly as to the amount of chloroform present. The specific gravity is an excellent criterion in this respect and a minimum figure of 1.065 at 25° C. would practically insure uniformity with the U.S.P. formula. A ready method of approximately estimating the chloroform, which is separated from the preparation by the simple addition of water, is offered by the following:

Thirty c.c. of chloroform liniment, placed in a 100 c.c. graduated cylinder and diluted to a volume of 100 c.c. by the addition of water, after thorough agitation followed by subsidence for at least one hour, should show a substratum of heavier liquid (chloroform containing some volatile oils, etc.) of not less than 9.5 c.c. at 25° C.

*Liquor Chlorig Compositus*.—A method for the valuation of this preparation as to the amount of free chlorine should be included.

*Liquor Magnesii Citratis*.—Absence of magnesium sulphate should be one of the additional requirements for this preparation. The test for barium chloride in the preparation after acidulation with hydrochloric acid is satisfactory for this purpose, if a slight turbidity but no definite precipitate is the requirement. It would be still more satisfactory to follow this up with directions for making a quantitative estimation of the magnesium present and establish a rubric for the minimum amount of magnesium, expressed as magnesium pyrophosphate or calculated back to the official magnesium carbonate, although the former would be preferable. As the formula now stands, this would lead to a requirement of 4.1 Gm. of magnesium carbonate in each 100 c.c. of finished preparation or 3.56 Gm. in each 100 c.c. when expressed as magnesium pyrophosphate.



*Liquor Potassii Hydroxidi.*—Absence of more than traces of potassium carbonate should be insisted upon in the preparation, which undergoes a deterioration of this kind quite readily. A proper method for filtration should also be given, in consequence of the frequent necessity for removing flakes of siliceous matter which are often found floating in the liquid.

*Liquor Sodii Hydroxidi.*—The same suggestions made with reference to liquor potassii hydroxidi are applicable to this preparation also.

*Massa Ferri Carbonatis.*—A requirement for the minimum per cent. of ferrous carbonate is just as important for this preparation as for ferri carbonas saccharatus, and a similar method for its determination should be included.

A minimum limit of 40.00 per cent.  $\text{Fe}_2\text{CO}_3$  would be satisfactory, as 41.70 per cent. is the amount theoretically present according to the formula given, and in the examination of a large number of commercial samples of this article none has ever been found to be below 40 per cent. except where it had deteriorated through age and improper keeping.

*Massa Hydrargyri.*—A purity rubric, together with a method for estimating the amount of metallic mercury, should be included for this preparation.

*Mel.*—The test for absence of cane sugar in honey is too rigid. Honey normally contains cane sugar to the extent of 7 per cent. at times.

A test for added invert sugar should be given, as commercial honey is frequently adulterated with this substance. There is one establishment, within the knowledge of the writer, making invert sugar in 4000 lb. lots for the sole purpose of adding it to honey. The added invert sugar always contains furfural and can readily be detected by applying the aniline acetate test for furfural, as follows:

When a mixture of aniline 1 c.c., glacial acetic acid 1 c.c., and water 2 c.c. is allowed to flow down the side of a test-tube in which several c.c. of a mixture of equal parts of honey and water have been placed, so as to form a supernatant layer, no red or pink zone should develop at the point of contact of the liquids within fifteen minutes.

*Oleatum Atropinæ, Oleatum Cocainæ, Oleatum Quininæ and Oleatum Veratrinæ.*—There should be processes of assay given

under each of these preparations, together with satisfactory tests for the identification of the separated alkaloid.

*Oleoresina Zingiberis*.—A test for capsicum should be included in the requirements for this preparation. Many commercial samples used in making ginger ale extracts contain capsicum and these occasionally find their way into the pharmaceutical trade. The method already given under fluidextractum zingiberis is satisfactory, using 1 c.c. or 1 Gm. of oleoresin of ginger in place of the 5 c.c. of fluid-extract, the other quantities and the manipulation remaining the same.

*Pilulæ Ferri Carbonatis*.—The same requirements for a minimum percentage of ferrous carbonate are applicable here as in the case of massa ferri carbonatis, previously referred to. Theoretically 21.73 per cent. by weight of ferrous carbonate is present. Practically it never is found to be below 20 per cent. nor should a lower amount than this be permitted.

*Pulvis Acetanilidi Compositus*.—Methods for the estimation of the several constituents in this preparation are necessary, in view of the importance of accurately declaring acetanilid under the various laws.

*Sodii Phosphas Exsiccatus*.—A method for estimating the moisture usually found in commercial samples of this salt is desirable.

*Spiritus Ammoniae Aromaticus*.—A minimum degree of alkalinity, preferably calculated as gaseous ammonia, would be an advantage for this preparation, which is very prone to deteriorate.

*Spiritus Camphoræ*.—The specific gravity of this preparation should be stated. A method for the determination of camphor should be given. The following is suggested:

Spirit of camphor should have an optical rotation of not less than  $+12.2^{\circ}$  when observed in a 100 mm. tube in a polariscope having a sugar scale. Or:

The angular rotation of spirit of camphor observed in a 100 mm. tube, when divided by .442, will give the number of grammes of camphor in each 100 c.c. of the spirit.

*Spiritus Menthae Piperita*.—The specific gravity of this preparation should be stated. A method for the determination of alcohol should be included, and that given in the Bulletin 107, A.A.O.A.C. for flavoring extracts containing volatile oils is very satisfactory.

A method for the determination of the volatile oil is also necessary. In view of the fact that most of the published methods re-



quire the use of a centrifugal machine and special flasks, the writer made some experiments with the view of utilizing the cassia flask which is already included in the equipment necessary for applying the U.S.P. tests. The following has given excellent results,—the only disadvantage being the time required to effect separation in the absence of a centrifuge:

Twenty-five c.c. of spirit of peppermint are transferred to a cassia flask and 5 c.c. of hydrochloric acid thoroughly mixed with it. The flask is then gradually filled with warm water (70° C., 158° F.), thoroughly agitating and rotating to dislodge the globules of oil which adhere to the sides of the flask. After standing for twenty-four hours the flask is again rotated to dislodge any additional globules of oil which have collected on the sides, after which the separated volume of oil is read off. It should not show less than 2.5 c.c. of oil of peppermint by this method, corresponding to 10 per cent. by volume of oil in the preparation. This same method is applicable for the determination of oil in several of the other official spirits, such as anise, cinnamon, lavender, and spearmint.

*Spiritus Frumenti.*—The “Marsh” test for caramel in whiskey should supersede the fullers earth test, which is unreliable.

*Syrupus Ferri, Quininæ et Strychninæ.*—A method for the separation of the quinine and strychnine, as suggested under elixir ferri, quininæ et strychninæ phosphatum, is also necessary in this preparation.

*Tinctura Iodi.*—A purity rubric for iodine and potassium iodide is necessary. A method for the determination of alcohol and also for the detection of wood alcohol should be given.

A method for the determination of potassium iodide is advisable. The following is suggested: 5 c.c. of tincture of iodine, evaporated on a water-bath in a tared dish, continuing the heating after subsequent additions of water until all of the iodine is volatilized and a white residue remains, should yield a residue of not less than 250 milligrammes, which should conform to the tests of identity and purity given under potassii iodidum.

*Tinctura Zingiberis.*—A test for the presence of capsicum is advisable. The test as given under fluidextractum zingiberis is applicable, using 10 c.c. of tincture of ginger instead of the 5 c.c. of fluidextract of ginger there directed.

## MANUFACTURE OF U.S.P. CHEMICALS AND CRITICISMS OF U.S.P. TESTS FOR THE SAME.\*

BY GEORGE D. ROSENGARTEN.

The Pure Food and Drugs Act of 1906, which made the U.S.P. a legal standard, naturally brought about a decided change in conditions surrounding the manufacture of U.S.P. chemicals. While the manufacturers have always desired to attain the highest purity possible for their products, it was found that it was not practicable in many instances to comply with the U.S.P. requirements. This condition, however, was largely overcome by the "Corrections and Additions" to the Pharmacopœia during 1907 and it is eminently proper to state here that the Committee of Revision gave every consideration to the mass of material that was put before them, and now, as a matter of fact, the requirements of the present Pharmacopœia, with some few exceptions, are comparatively readily attained, at least as far as chemicals are concerned.

There is, however, still ample scope for revision, and there is no question that the study of all the subjects relative to the U.S.P. and medicinal chemicals in general, owing to increased responsibilities, will be given greater attention, and the future possibilities which are open to this very interesting and broad field are of the greatest importance.

The purity rubric, which has proved to be one of the best innovations in the Pharmacopœia, gives the chemicals whenever it is possible a certain definite standard, and if in all instances the limitations of dangerous impurities are absolutely fixed by well-defined and sure tests or analyses, the presence of small quantities of innocuous substances may be permitted. Small percentages and traces of such innocuous substance, which were required to be eliminated by former Pharmacopœiæ, made the production of U.S.P. chemicals exceedingly arduous, and naturally increased the cost, which eventually had to be borne by the consumer. This can readily be understood by a simple case, taking, for example, sodium phosphate, which if made C.P. as virtually required by the U.S.P. 1890, commands a much higher price than the salt of the U.S.P. 8th Revision, which

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\* Read before the Scientific Section of the Philadelphia Branch of the American Pharmaceutical Association, November, 1909.

requires 99 per cent.  $\text{Na}_2\text{HPO}_4 + 12\text{H}_2\text{O}$  and allows small quantities of innocuous impurities which in no way impair its therapeutic value.

However, the official description must be made so clear that there can be no question concerning poisonous and undesirable impurities, and when a chemical in question complies with the purity rubric, it certainly fulfils the Pharmacopœial requirements. A number of questions have been raised concerning this very point, and it undoubtedly was the intention of the Committee of Revision, that the purity rubric should cover the case, that when a substance is free from deleterious matters and meets the percentage required by the rubric, it complies fully with the meaning of the text.

Melting and boiling points have already been freely discussed, and there is no doubt that, as a criterion for purity of many substances, the Pharmacopœia must insist on their use for this purpose. However, it is very necessary that uniform methods should be required for their determination, and this also applies to solubilities, as experience has shown that cases have occurred where variations have been noted. Is the solubility determined by dissolving the specified quantity of the chemical in the required amount of the solvent, or is it determined by the amount of the chemical remaining in the saturated filtered mother-liquor? In the case of some alkaloïds and their salts discordant results have been found, and there is evidently no question but that there should be careful revision to meet such instances.

Ash and residue determinations have been a source of considerable discussion in the laboratory. When it is stated that there should be no weighable residue, and there is no definite quantity given, it depends a great deal on the operator whether or not this requirement is fulfilled. It is also necessary in cases where evaporation is required to take the actions of the various chemicals on glass and porcelain into consideration, as the residue may be increased manifold if this necessary precaution is neglected. A platinum crucible for these determinations is not mentioned in any instance in the U.S.P., and the reason is obvious, as all of us are not in possession of such a valuable piece of apparatus, but for accurate work platinum is required. There have been instances reported of examinations of chemicals, during which porcelain crucibles were used, with the result that finally impurities were in evidence that were not present in the original substance.

The personal equation as an eminent factor goes without saying, and all lines should be drawn to cut this factor down to the smallest possible limitation of variations, so that unnecessary discussions and correspondence may be eliminated. It is necessary to have all definitions and tests made so precise that there can be no question, and the best and uniform methods should be adopted from time to time as occasion may arise, so that there may be concordant results. It is well understood, of course, that complete laboratory work cannot always be accomplished by all, but finally all the onus really comes on the manufacturer, and consequently every possible precaution is taken to protect the consumer. The productions of the laboratory are subjected to tests by chemists who have nothing to do with the manufacturing of the chemical, and, in addition, the product is not allowed to leave any department of the laboratory until the actual manufacturer is satisfied that it is correct in every particular. A record is kept of every lot, and its history may be traced from the time of its production until the time when the label bearing its particular mark is destroyed.

The question of proper apparatus for the manufacture of medicinal chemicals is sometimes very perplexing. There are at command glass, quartz, porcelain, earthenware, enamelled, metallic, and vessels of every description, but the decision as to which is best for the purpose can only be reached by long experience, and even then it is necessary to use great precaution, so that the resulting product may be of the proper purity, and it is often necessary that complex apparatus be used in order that all requirements may be met.

That all manufacturers desire that their various products coming under the head of "white chemicals" should be of the whitest is self-evident, and since the limit of iron, which is practically always present, was very much increased in the heavy metal test, it is possible to use such apparatus which otherwise would necessarily have been eliminated. Iron is almost always the cause of "off-color," but with the proper care its effects can be overcome, and even the most critical, of whom there are multitudes, can be satisfied. A more difficult proposition is the presence of mechanical impurities,—atmospheric dust, particles of carbon, milling dust, fibres from filtering and drying materials, small pieces of wood from containers, being everlasting sources of annoyance, and, in fact, it is very difficult at times to convince all that it is impracticable to manufacture material by



the ton, to mill it to a fine powder, and still obtain an absolutely clear solution.

Deterioration is another condition which arises where the natural and unavoidable change in many chemicals is concerned. Alkaloids, for instance, when subjected to light, or by age, change color yet may not lose any of their efficiency, whereas, on the other hand, such chemicals as sulphites, ammonium carbonate, etc., are undoubtedly considerably affected by such changes which occur in spite of all precautions. It is evident that the manufacturer cannot guard against such deteriorations, since they follow natural courses, but can only protect himself as far as possible by applying chemical knowledge and good common sense.

A few comments on some of the Pharmacopœia tests may be of interest:

*Acetphenetidin*.—To determine the presence of acetanilid, acetphenetidin is boiled with sodium hydroxide, the solution cooled, agitated with chlorinated soda solution, when a clear yellow liquid should result, and not a purplish red or brown red cloudy liquid or precipitate. Nevertheless, when making this test a precipitate is obtained, indicating the presence of acetanilid, although it could not be found by the bromine or other tests.

*Acid Acetic, Glacial*.—The test for empyreumatic substances is very strenuous. It is required that the tint produced by the addition of two drops of one-tenth normal potassium permanganate solution to 2 c.c. of the acid, diluted with 10 c.c. of water, should not be changed to brown within two hours. The German Pharmacopœia requires that when 5 c.c. of acid in 15 c.c. of water are mixed with 1 c.c. permanganate of potash solution (1-1000) it should not lose its red color within ten minutes.

*Calcium Bromide*.—If a quantity of this salt is used in testing for bromates, and only a drop of diluted sulphuric acid, a yellowish color may be developed, but in such instances bromates could not be detected by any further tests. However, if the salt is covered with diluted sulphuric acid no color results.

*Calcium Phosphate*.—The limit for chlorides is exceedingly difficult to attain.

*Cinchonine Sulphate*.—It is stated that one part is soluble in 69 parts of chloroform at 25° C., and further on there is a requirement that: "If one part of the powdered salt be macerated with frequent agitation in 80 parts of chloroform, at ordinary tempera-



tures, it should be wholly or almost wholly dissolved (limit of quinine or cinchonidine sulphate)."

*Collodion*.—The U.S.P. 8th Revision requires 40 Gm. gun-cotton to be dissolved in 750 c.c. ether and 250 c.c. alcohol, whereas the U.S.P. 1890 required only 30 Gm. in the same amount of solvents. The increased quantity of gun-cotton has caused some trouble where collodion is used as a base for preparations.

*Glycerin*.—It is apparently difficult to eliminate the last traces of butyric acid. In almost every examination of glycerin a fruity odor is noticed when treated with alcohol and sulphuric acid.

*Iron Chloride Solution*.—The test for oxychloride is not sufficiently exacting. It has been found that when tincture iron chloride is made from a solution which meets the oxychloride test, the tincture subsequently becomes turbid owing to an excess of oxychloride.

*Lime, Sulphurated*.—The test for the percentage of pure calcium sulphide is somewhat misleading, as there is always iron present, which will, on the addition of ammonia, impart a brownish color to the filtrate.

*Mercury Oxide Yellow*.—Criticism has been made that mercury oxide yellow contained red oxide, because it is not entirely converted into white mercuric oxalate when digested on the water-bath with oxalic acid for fifteen minutes. Experiments show that even if the yellow oxide is reduced to a very fine powder, a small portion still remains unchanged, consisting of minute lumps of a fine yellow powder, showing no crystalline appearance under a lens magnifying four diameters. This residue was not converted to oxalate even after heating for several hours. When the yellow oxide is mixed with a small quantity of red oxide, and the same test applied, the residue shows a decided red color and crystalline structure. When red oxide of mercury is powdered until it becomes the same color as yellow oxide, there is a partial conversion into oxalate at the end of fifteen minutes, but when treated with oxalic acid without powdering, there is no visible diminution of the red color at the end of two hours.

*Sugar of Milk*.—Even the corrected test has given considerable trouble in testing for cane sugar, and is difficult to comply with. However, when the test of the German Pharmacopœia is applied, samples which meet the other U.S.P. requirements stand the German test perfectly. This difference is occasioned by the fact that the U.S.P. requires diluted alcohol containing about 41½ per cent. by

weight, while the "Verduenter Weingeist" of the German Pharmacopœia contains 60 to 61 per cent. by weight of alcohol. In this test the sugar of milk is digested with diluted alcohol and the filtered liquid should remain clear after mixing with equal volume of absolute alcohol, and if evaporated on a water-bath there should not be a greater residue than 0.03 Gm.

From all the foregoing it would seem that further study must be given to the Pharmacopœia. While it is desirable that a high standard should be set for all medicinal chemicals, in accordance with the steady advance of modern times, yet the requirements should not be fixed on a plane beyond practical attainment, and such tests for purity as may be established should be so well proven that they will show the correct result when properly applied.

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## HISTORY OF MACERATION AND PERCOLATION.\*

BY OTTO RAUBENHEIMER, PH.G., Brooklyn, N. Y.

In connection with this symposium held at the oldest College of Pharmacy in the U. S. it occurred to me that a historical sketch on maceration and percolation might be of interest to the members.

### MACERATION.

Etymology of the word: In Latin it is *maceratio*, the art of soaking, derived from *macero*, to make soft, to soak, which again is derived from *macer*, lean or meagre.

This process has been in use from times immemorial.

The earliest known solvents in ancient times, besides water, were wine and wine vinegar.

Wine, as we all know, has been and is to-day used as a beverage by all nations, with the exception of the Mohammedans, being prohibited by the Koran on account of its intoxicating properties. (I am, however, informed that the Sultans drink champagne, which they do not consider as a wine.) As a medicine, wine has been and is to-day used over the entire world, and medicated wines have been employed in ancient times and continue to hold their place in the various pharmacopœias of the present.

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\* Read at the November Pharmaceutical Meeting, Philadelphia College of Pharmacy.

The most important solvent in classic times was undoubtedly vinegar, obtained through the acetic fermentation of wine. The ancients had the most extravagant ideas with regard to the solvent power of vinegar, not only upon vegetable but even upon mineral substances, as may be gathered from the concordant statements of Livy and Plutarch that Hannibal, the celebrated Carthagenic general, in his passage across the Alps, cleared the way of rocks by means of vinegar. I might also quote here the story which Pliny tells of Cleopatra, who in fulfilment of her wager to consume a million sesterces at one meal, dissolved some costly pearls in vinegar and drank the solution.<sup>1</sup>

The acid plant juices were assumed by the ancients to contain vinegar, and naturally medicated vinegars were prepared by maceration and are still official in the present pharmacopœias. The Father of Medicine, the Greek physician Hippocrates, in the 5th to the 4th century B.C., already prepared acetum scillæ, vinegar of squill.<sup>2</sup>

You will ask why did the ancients not use alcohol, the great solvent, and macerate therein the various drugs, etc.? My answer to this is, that, strange as it may seem, alcohol was unknown in ancient times. Not until about 1100 is the distillation of spirit from wine mentioned by Khalaf-Ebn-Abbâs Abul Kasan. Raimundus Lullus (1235-1315) named this spirit "Aqua Ardens," from ardere, to burn, burning water, a name still in use as the "Branntwein" of the Germans and the "fire water" of our Indians. A very important event in pharmaceutical history is, that Lullus was the *first* to prepare tinctures and quintessences by macerating the different drugs in spirit.<sup>3</sup>

But not until the 16th century did these preparations come into more general use through Phillipus Aureolus Paracelsus Theophrastus von Hohenheim, that much abused and envied physician-pharmacist, chemist, philosopher, and theosoph, the founder of iatro-chemistry (medical chemistry), which in contrast to alchemy opened new paths in chemistry and medicine by joining these two sciences. Paracelsus gave a tremendous impetus to the higher development of the apothecary's calling by his generous additions of chemicals as well as tinctures, essences, and quintessences to the *materia medica*. Before his time apothecary shops were nothing more than stores for roots, herbs, syrups, plasters, cerates, and especially confections. The service which Paracelsus rendered in instigating physicians and apothecaries to busy themselves with

chemistry, etc., was indeed a great one, and A. N. Scherer in his memoir "Theophrastus Paracelsus" (St. Petersburg, 1821) rightly says: "Pharmacy owes *everything* to Paracelsus."

In olden times the apothecary collected his own drugs, roots, herbs, flowers, etc., in the proper season, and he himself prepared his waters and spirits by distillation and his tinctures by maceration. The collection of drugs by the apothecary kept him in touch with botany and pharmacognosy and was especially very educational to the young pharmacist and is far superior to the selling of herbs, flowers, and even roots of *doubtful value* in *pressed packages*, as practiced by the average druggist of to-day. The old apothecary carried on this maceration in glass bottles or jars in the front window of his shop, so that the sun would strike and thereby warm the preparations. The resulting different colored tinctures very correctly can be styled as giving origin to the colored show bottles in our windows to-day.

I beg to remind the users and advocates of maceration that agitation must not be forgotten, and I know as a fact that it is very often forgotten in this process. For obvious reasons frequent agitation, at least once a day, is essential. It might be of interest to learn that the second edition of the Netherland Pharmacopœia 1871, in the preparation of its tinctures even ordered *continual* agitation ("agitatio continua") for 7 to 28 days! If our admirers of this so-called *simple* and *labor-saving* maceration would have to practice the Dutch method, then I believe they would soon reach a different conclusion.

Expression must necessarily go hand in hand with maceration, especially in the case of bulky drugs, as f. i. arnica flowers, in order to remove the liquid from the marc as much as possible. This, however, can never be accomplished entirely, and the retention of *strong* menstruum in the marc and the resulting indefinite finished preparation are the chief objections to the process of maceration. To overcome these, several pharmacopœias, the Hungarian, the Rumanian, the British, and the U. S., order the expressed marc to be remacerated with menstruum and then to be expressed again so as also to obtain a definite quantity of the finished preparation, as f. i. in Tinctura Arnicae U.S.P. VIII. As the resulting liquid will be very turbid it must, last of all, be filtered. So you can readily see that the so-called simple process of maceration consists of maceration, agitation, expression, remaceration, and filtration, not so simple after all.



The *disadvantages of maceration* can be briefly summed up as follows: (1) the shaking; (2) the expressing and filtering; (3) the retention of strong menstruum in the marc and the indefinite finished product. The *advantages of maceration* are said to be: (1) the drug does not have to be a fine and uniform powder; (2) the process requires less skill and care in the manipulation than percolation; (3) there is less loss of alcoholic menstruum than by percolation.

Before leaving the subject of maceration I will say a few words about digestion, not Cleopatra's digestion, as cited before, but *pharmaceutical* digestion. Latin: digestio, derived from digerere, to distribute, which is a maceration carried on at a higher degree of temperature. Some of the pharmacopœias specify the temperature as:

	Ph. Ned. IV	Ph. Aust. VIII	U. S. P. VIII
Maceration .....	15°-25°	not over 20°	15°-20° in a shady place.
Digestion .....	35°-45°	not over 50°	
Infusion .....	90°-98°		

If a higher temperature is employed, as in the case of Warburg's tincture N.F. III (65°), it is best to attach an upright or reflux condenser or simply a glass tube about 4-6 feet long, so as to prevent the loss of alcohol.

#### PERCOLATION.

Etymology: per, through, and colare, strain.

A vast volume of literature exists on this interesting subject, and the brightest minds of all nations have spent a "lifetime of labor" in trying to perfect percolation and to enlighten us. Among these the following deserve special mentioning: Boullay, Robiquet, Guillermond, Pelletier, Pelouze, and Soubeiran of France, where percolation is said to have been originated, which, however, I find to be fallacious; Redwood, Proctor, Maben, and Ince, of Great Britain; Dieterich, Geiger, and Marpmann, of Germany; Duhamel, Procter, Parrish, Grahame, Squibb, Diehl, Oldberg, Lloyd, and Remington, in the United States. The American Pharmaceutical Association and the Philadelphia College of Pharmacy are to be congratulated upon the many faithful workers, whose contributions on percolation have been published in the Proceedings of the A.Ph.A. and first of all in the AMERICAN JOURNAL OF PHARMACY.

The oldest forerunner of percolation was undoubtedly the *lixiviation* (from lix, ash) of the ashes of plants. Aristotle, of Athens,

384-322 B.C., the celebrated Greek philosopher and founder of the peripatetic school, already described this process of obtaining crude potash. According to the plants used the resulting salt—*Sal lixivius*—was named as *Sal absinthii*, *Sal cardui benedicti*, etc. Lixiviation or leeching (German-Auslaugen) has been extensively practiced in various technical industries ever since. Even to-day the new Spanish and French pharmacopœias give the percolation process the name lixiviation and the French Codex devotes two and a half pages (383-385) under the title "*Lixiviation*."

In 1746 Comte Claude-Toussaint-Murot de la Garaye (1675-1755) published a work in Paris: "*Chymie hydraulique pour extraire les sels des végétaux, animaux et minéraux par moyen de l'eau pure*," in which he advocated and described the extraction of powdered vegetable drugs, etc., with water. "*Sel*" was not merely the name for a chemical salt but also for an extract or active principle, as can be seen by the old synonym "*Sal essentielle tartari*" which stands for tartaric acid. One of the products of the chemical and pharmacological studies and researches of this French physician and philanthropist was the preparation of the so-called "*Sal essentielle de la Garaye*," which was a dry cinchona extract.<sup>4</sup> But already in 1672 the German "*Chymicus*," Joel Langelot or, as it was customary those days, Latinized to "*Langelottius*," the alchemist and Court physician to the Duke of Schleswig-Holstein, recommended the very same method and also constructed a "*philosophical mill*" described by Joh. Christ Wiegleb, *Geschichte des Wachstums und der Erfindungen in der Chemie* (Berlin and Stettin, 1791-1792). This is by rights the forerunner of the method of displacement.

Benjamin Thompson, Count of Rumford, a born American (at Rumford now Concord, N. H.), who deserves special credit for being the first to ascertain that liquids can be boiled by means of steam, used a method of preparing coffee, resembling our present percolation, which he described in his 18th essay in *Repertory of Arts*, April and May, 1813.

In 1817 C. Johnson applied this principle to the extraction of cinchona bark in England, saying: "The machine I use is similar to the one made several years ago by Edmund Loyd & Co., 178 Strand, London, and does not differ essentially from any of those described by Count Rumford. In the Lancaster public dispensary this method is found to yield a better preparation than was formerly obtained from twice the quantity of cinchona bark" (*Annals of Philosophy*, ix, p. 451).

In 1816 the French Count Réal invented a hydrostatic extraction press or pressure percolator in which the drug is held in place by perforated disks and the solvent, contained in a tube twelve feet high, is forced through by its own pressure. Réal's process and apparatus are described in *Annalen der Pharmacie*, vol. xv, p. 80, also in Buchner's *Repertorium* and in Soubeiran's *Traité de Pharmacie*, the German translation by Schoedler which I have here for your inspection devoting seven pages (pp. 123-129) to this subject. On pages 127 and 128 the fineness of the powder and the method of packing are described by Soubeiran and the German pharmacist Geiger. Philip Lorenz Geiger, the discoverer of a number of alkaloids, as coniine, atropine, hyoscyamine, aconitine, and colchicine, also wrote a little book, *Réal's Aufloesungspresse*, Heidelberg, 1817.

A very important point in Réal's process is that he recommended to macerate the ground drug with 50 per cent. menstruum for several hours before packing it in the apparatus. No doubt the Réal process smoothed the way for the coming percolation method.

In 1834 the French pharmacist Theophile Jules Pelouze employed the process of displacement in his laboratory by extracting nutgalls in the preparation of tannic acid.

In 1835 the French pharmacist Boullay and son (the father discovered picrotoxin in 1818) published in the *Journal de Pharmacie*, vol. 21, pp. 1-22, their paper: "Considerations nouvelles sur la méthode de déplacement,"<sup>5</sup> giving the experience of Soubeiran, Limonin, Boudet, Buchner, Dublanc, Pelletier, and Pelouze. In the same journal, p. 113, Robiquet criticizes Boullay's claims to priority, having used the méthode de déplacement for five to six years in his laboratory and factory. I beg to point out that in Boullay's method the drug was put dry into the apparatus.

Dr. Fr. Schoedler, the translator of Soubeiran's *Traité de Pharmacie*, states, p. 115: "The science of pharmacy has *not* been enriched through the much praised méthode de déplacement of M. Boullay nor through the experiments of Guillermond. The principle and application of their method are the same as the Réal process, which has been in use over twenty years."

An abstract of the paper of M. A. Guillermond was reported as early as 1836 in the AMERICAN JOURNAL OF PHARMACY, vol. vii, p. 308, and I am glad to state that this JOURNAL of the Philadelphia College of Pharmacy has been the recipient of the largest portion of the literature on percolation ever since.

In 1838 the Philadelphia pharmacist, Augustine Duhamel, published in the A.J.Ph., vol. x, pp. 1-17, an essay, "Boullay's Filter and System of Displacement with Observations drawn from Experience." Duhamel deserves special credit, as he was the first to present this subject to the American pharmaceutical profession.

In 1839 A. Duhamel and Wm. Procter, Jr., published in the A.J.Ph., vol. xi, pp. 189-201: "Observations on the Method of Displacement," in which paper they state that in France this method is extensively applied and was *made official* in the *Codex 1835*, but in the U. S. it is hardly known, much less applied, and they make a plea for its introduction into the next U.S.P. And it was introduced into the U.S.P. 1840, which authority states in the preface: "As to the *kind of filtration commonly called displacement*, it is strongly recommended to those who have not made themselves practically familiar with the various sources of error in the matter of displacement to postpone its application whenever an alternative is given in this work, until they shall have acquired the requisite skill."

In 1840 this process was also sanctioned by the Edinburgh Pharmacopœia, which states: "A much superior method has been introduced which answers well for most tinctures—namely the *method of displacement by percolation*." This is the first mentioning of percolation, which word is used instead of displacement. Quite a dispute arose which pharmacopœia adopted percolation first. As a matter of fact it was made official in both pharmacopœias in their edition of 1840, but the U.S.P. 1840 did not appear until 1843 and the Edinburgh Pharmacopœia 1840 was published in 1839.

As we have seen before Réal moistened the ground drug with half its weight of menstruum, Boullay used the dry powder, and the Edinburgh Pharmacopœia moistened it sufficiently with menstruum to form a thick pulp.

The British Pharmacopœia of 1864 in which percolation was introduced gives the following, according to Ince *very unsatisfactory*, general directions: "Macerate for forty-eight hours in three-quarters of the spirit in a closed vessel, agitating occasionally; then transfer to percolator and when fluid ceases to pass, continue the percolation with the remainder of the spirit." Such an authority as Ince criticizes this method as *unnecessary, wasteful, and messy*. As this combination method is even used to-day by some druggists, I hope they will consider these criticisms and discard this process in favor of the up-to-date percolation method.



Before the A.Ph.A., in 1858, Prof. Israel G. Grahame read an excellent paper: "The Process of Percolation or Displacement, its History and Application to Pharmacy,"<sup>6</sup> in which he makes the following remarks which still hold good to-day: "If I have a just conception of the principle upon which it is based, it is, that the substance to be treated and the menstruum should be presented to each other under such circumstances, that *each particle of the solvent shall be fully charged with soluble matter and immediately displaced with another particle*, to become in its turn saturated in a like manner; and if all the conditions of the process have been properly observed, these saturated particles collect and escape from the apparatus, and contain to the fullest possible extent all that the *menstruum is capable of taking up and even more than could be taken up by any other means.*" Prof. Grahame, aside from suggesting the use of the funnel as a percolator, deserves credit for advocating the use of powdered drugs of regular and definite degree of fineness, as well as the proper moistening before packing it in the percolator; both of these suggestions are even now considered indispensable to successful percolation.

A committee of the A.Ph.A., consisting of E. Parrish, I. J. Grahame, and C. T. Carney, presented a report on percolation at the 1859 meeting, giving an account of the introduction of the *kind of filtration commonly called displacement* into U.S.P. 1840, its extended use in U.S.P. 1850, and a proposed general description of *percolation* for U.S.P. 1860.<sup>7</sup>

Four pages (pp. 3-6) are devoted to percolation by U.S.P. 1860, "The kind of filtration known as percolation or the process of displacement," the use of a funnel being also permissible and the uniform powder being moistened with one-quarter to one-half its weight of the menstruum. In U.S.P. 1870 we find the same general description (pp. 3-6), with the exception that the powder is to be moistened with a *specified quantity* of the menstruum. In U.S.P. 1880 and 1890 this chapter has been improved by giving more explicit directions, by passing the moistened powder through a sieve, by the attachment of a long rubber tube to the percolator to regulate the flow, by directions to percolate the dregs of a tincture, and by authorizing repercolation in the preparation of fluidextracts. In U.S.P. VIII this chapter has been further improved by dividing it into distinct paragraphs, as percolators, the process, repercolation, rate of flow, and maceration, stating under the latter that percolation

is not suitable for exhausting some drugs and that the process of maceration is employed for some of the tinctures as aloes, asafetida, sweet orange peel, etc.

U.S.P. VIII has made a number of improvements in the manipulation of the percolation process. The quantity of menstruum to moisten the drug has been reduced, f. i. tinct. hydrastis: U.S.P. 1890 used 150 c.c., and U.S.P. VIII only 60 c.c.; tinct. cinchon co. U.S.P. 1890 used 200 c.c., and U.S.P. VIII only 80 c.c. Furthermore the U.S.P. 1890 directed to macerate the moistened drug for twenty-four hours and then pack it in the percolator and proceed with percolation. The U.S.P. VIII has made a great improvement in the macero-percolation process by directing to transfer the moistened drug to the percolator and, without pressing, allow it to stand, well covered, for six or in some cases twelve hours, then pack it firmly, pour on the menstruum, and when the liquid begins to drop close the lower orifice and macerate again from twenty-four to forty-eight hours and then allow the percolation to proceed slowly, in the case of tinctures from eight to fifteen drops per minute. This rate of flow in the new Swiss Pharmacopœia is twenty drops per minute, in the new Austrian Pharmacopœia thirty drops, and in the German Pharmacopœia (under *extracta fluida*) forty drops per minute. The new French Codex states that the twenty-four hours' percolate should weigh about one and a half times the amount of drug employed.

The fruitful work which Dr. E. R. Squibb has done as to percolation requires no further comment.

Repercolation or fractional percolation as called by Prof. Diehl was introduced by Squibb in 1866 with the object of saving alcoholic menstruum and to prepare strong solutions, as fluidextracts, without the application of heat. The origin of fluidextracts is generally credited to American pharmacy, and the work of Grahame,<sup>8</sup> Procter,<sup>9</sup> Squibb,<sup>10</sup> and others is well known. The U.S.P. 1850 recognized seven fluidextracts, 1860, twenty-five, 1870, forty-six, 1880, seventy-nine, 1890, eighty-eight, and U.S.P. VIII, eighty-five, now under the official title "*Fluidextractum*." Besides this, fluidextracts have become official in almost all pharmacopœias and are recognized as "liquid extracts" in the British Pharmacopœia.

Percolation is also gradually but steadily replacing maceration in the foreign pharmacopœias. Chapters on percolation, similar to the U.S.P. process, are adopted in these books and general formulas

for fluidextracts and tinctures are given. The greatest victory, however, which percolation has gained is its recognition by the Brussels International Conference for the Unification of Pharmacopœial Formulæ for Potent Medicaments, a copy of which can be found in that excellent "Digest of Comments on U.S.P.", Bulletin No. 49, Hygienic Laboratory, by Murray Galt Motter and Martin I. Wilbert, pp. 64-68. Article 2, b, of the Protocol states: "Tinctures of potent drugs shall be prepared of the strength of 10 per cent. and by *percolation*." September 20, 1902, the day on which this agreement was signed, will be a memorable one in the annals of pharmacy—it marks the advent of a new era, the attainment of attempts covering nearly fifty years to unify the formulæ for potent medicaments throughout the world. It might be of interest to learn that when this Protocol was signed again by the duly authorized representatives of the various governments on November 29, 1906, at the Belgian ministry for foreign affairs, the Swedish government formulated the following reservation: "As the preparation of tinctures of drugs by percolation involves an increase in the price of these products, this method seems not altogether suitable for employment in a general manner in Sweden."

In connection with this subject it might be of interest to learn that the new Austrian and Swiss Pharmacopœias order tincture of opium to be prepared by maceration instead of percolation, the latter authority calling attention to this in a footnote. The new French Codex, by the way, orders this tincture to be prepared by dissolving 5 Gm. of extract of opium in 95 Gm. of 70 per cent. alcohol. Our U.S.P. VIII seems to have solved this problem in an excellent manner, by first extracting the opium with boiling water, then macerating in diluted alcohol, and lastly percolating.

In summing up I want to say that the disadvantages of maceration, *i.e.*, the shaking, expressing, and filtering, the retention of strong menstruum in the marc, and the indefinite quantity and strength of the finished product, are the principal advantages of percolation. The advantages of maceration are very little indeed. The uniform fineness of the ground drug used in percolation can be easily regulated by the sieve. The necessary skill and care in the manipulation of the percolation will certainly be acquired by the college teaching and principally by the practical experience, and I beg to remind you that the clerk who cannot conduct percolation properly ought not to be employed. As to the increased loss of alcoholic

menstruum by percolation, being left in the marc, the same can be expressed, distilled, or displaced by water.

In my experience the percolation process, and especially the improved macero-percolation method of our U.S.P. VIII, although the same cannot be used for the exhaustion of all drugs, decreases the labor and saves time and is a scientific method par excellence. When properly carried on all the advantages of maceration are obtained and furthermore it is superior to maceration, inasmuch as no strong menstruum is retained in the marc.

In conclusion I want to state that, although percolation has been originated in a foreign country, American pharmacists have greatly perfected this process and American pharmacy can justly be proud of it.

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<sup>1</sup> Meyer-McGowan, History of Chemistry, 1906, p. 21.

<sup>2</sup> Schelenz, Geschichte der Pharmazie, 1904, p. 104.

<sup>3</sup> *Ibid.*, p. 328.

<sup>4</sup> *Ibid.*, p. 566.

<sup>5</sup> Journal de Pharmacie, 1835, vol. 21, pp. 1-22.

<sup>6</sup> Proc. A.Ph.A., vol. 7, pp. 285-294, and A.J.Ph., vol. 31, p. 354.

<sup>7</sup> *Ibid.*, vol. 8, pp. 220-239.

<sup>8</sup> *Ibid.* 1858.

<sup>9</sup> *Ibid.*, 1863, vol. 11, pp. 222-248.

<sup>10</sup> *Ibid.* and Percolation by Brandel and Kremers, Ph. Review, 1906, p. 363, 1908, p. 270.

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#### MAHLON N. KLINE.

Mahlon N. Kline, President of the Smith, Kline & French Co., wholesale druggists, Philadelphia, died suddenly of heart failure on Saturday evening, November 27, while attending a meeting of the Brotherhood of St. Andrew at the Church of the Saviour, Philadelphia. Mr. Kline was so long and so intimately associated with the drug trade, both wholesale and retail, and did such excellent work in connection with drug and pharmaceutical matters that his death will be felt as a distinct loss to the industry.

Of all his other affiliations it may truly be said that none were of more deep concern to him than his relations with the Philadelphia College of Pharmacy, and his work as a member and officer reflects credit alike on his ability and loyalty to its interests. He was elected an active member in 1886 and a member of its Board of Trustees in 1897, of which latter body he became Chairman in 1901. He was elected First Vice-president of the College in 1905,



and at the time of his death was also Chairman of the committees on legislation and finance of the College, besides holding other minor offices. Mr. Kline's interest in the College was also manifested in other ways. Since 1897 he had offered an annual prize of a prescription balance to the student passing the best examination in the theory and practice of pharmacy. He was liberal in contributing to the financial support of the College, and probably his most notable contribution was as a member of the Smith, Kline & French Co. in conjunction with Mr. Howard B. French in purchasing and donating the Martindale Herbarium, in 1894.

Mr. Kline was born February 6, 1846, near Hamburg, Berks County, Pennsylvania, and was educated in the public schools. In 1865 he went to Philadelphia and laid the foundation of his successful business career in the employ of the wholesale drug house of Smith & Shoemaker. His merit was quickly recognized and three years later he was admitted to partnership in the firm.

Mr. Shoemaker retired in 1869 and the name of the firm was changed to Smith, Kline & Co., which in 1888 was incorporated under the style of The Smith & Kline Co. In 1891 a wholesale drug business of French, Richards & Co. was liquidated and Harry B. French of this firm joined the Smith & Kline Co., as its Vice-president, the name being again changed to Smith, Kline & French Co.

Mr. Kline joined the National Wholesale Druggists' Association at the time of its formation in 1882 and in 1885 was elected its President. For ten years, from 1887 to 1897, Mr. Kline served conspicuously and efficiently as the Chairman of the Committee on Proprietary Goods, which he relinquished to assume the chairmanship of the Committee on Suits against members of the association. In this connection he had proved himself invaluable in shaping the course which was pursued in the "Park" suits and in the litigation which ultimately led to the "Indianapolis Decree." In 1898 at the annual meeting of the association held in St. Louis that year, he was made Chairman of the Legislative Committee, which position with but one year's interruption he retained up to the time of his death. While acting as Chairman of the Legislative Committee Mr. Kline was largely responsible for the passage of the denatured alcohol bill and it was through his efforts largely that the law permitting of the drawback allowance on grain alcohol for export when used in medicinal and

toilet preparations or by itself was passed. He was also largely instrumental in persuading the Commissioner of Internal Revenue to allow manufacturing druggists a free use of fortified sweet wines in compounding their preparations.

He was a staunch advocate of the Pure Food and Drugs Act and devoted much effort towards bringing about uniformity of State law to conform with it.

Mr. Kline always took an active interest in the affairs of the city of Philadelphia and was foremost in many of the municipal reform matters. He was a prominent member of the Trade League of Philadelphia, which afterward became the Philadelphia Chamber of Commerce, and he likewise served on the Executive Committee of the National Chamber of Commerce instituted by Secretary Straus.

Always alive to the interest of his retail friends of the drug trade, Mr. Kline was an active member of the Pennsylvania Pharmaceutical Association and had he lived would have represented that organization at the Pharmacopœial Convention to be held next May.

Mr. Kline was a devoted member of the Church of the Saviour from which he was buried on November 30. The funeral was largely attended and among those present besides the officers, members of the Board of Trustees, and faculty of the Philadelphia College of Pharmacy, was a substantial delegation from the National Wholesale Druggists' Association and various pharmaceutical organizations with which he was identified. In connection with his church affiliations Mr. Kline was the Philadelphia leader of the Brotherhood of St. Andrew.

Mr. Kline is survived by a widow, two daughters, Mrs. Harry F. Valentine and Mrs. T. Carrick Jordan, and one son, Clarence M. Kline.

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#### PHILADELPHIA COLLEGE OF PHARMACY.

A special meeting of the members of the Philadelphia College of Pharmacy was held December 10 to take action on the death of Mahlon N. Kline, First Vice-President and Chairman of the Board of Trustees.

*The President* read the call for the meeting which had been signed by seventeen members of the College and of the Board of

Trustees. He then said that in the death of Mr. Kline the College had lost one of its most able and energetic members; and as an officer the College had lost the services of a man hard to replace. He was a strong man, energetic, ready to assume any responsibility, and ready to work in any and all lines of duty. Personally his loss was a sad blow to him. The circumstance connected with his sudden death was a severe shock to him as he had been in consultation with Mr. Kline about College matters up to within four hours before his death. On this occasion Mr. Kline had advised him to take care of his health by taking a rest from business cares. His concern for others was a characteristic feature.

Communications were read from Professor L. E. Sayre, Mr. Frank G. Ryan, and Mr. C. Carroll Meyer, and a telegram from Mr. Wallace Procter, expressive of their appreciation of Mr. Kline and regret at his death.

In response to the call of the President for remarks a number of the members responded, as follows:

*Dr. A. W. Miller* stated that his acquaintance with Mr. Kline probably extended further back than most of those present. Their business relations brought them together almost daily for many years past, and Dr. Miller said that he always admired Mr. Kline's behavior in business affairs. He occupied a leading position in all the associations in the drug trade with which he was connected. Much of his energy was directed towards the legal questions concerning the trade. He had a singular aptitude in handling these questions and was of great service in all organizations with which he was connected. He had the highest feeling of respect for Mr. Kline, and his sudden death was a severe shock as it brought vividly to mind the uncertainty of life and the certainty of death, and as such a life should ever be kept in mind, he suggested that steps be taken to procure a portrait of Mr. Kline that should be displayed on the walls of the College.

*Professor Joseph P. Remington*, after referring to the illness of Mr. Kline, said:

"The almost tragic death of this noble man, occurring as it did in the church which he loved so well, while shocking to his family and friends possessed an appropriateness which develops in the mind after some time has elapsed for reflection. Mahlon N. Kline was a marvel for energy and ability, with a capacity for long persistence in grinding labor. He never shirked responsibility, and although

probably the majority of his tasks were distasteful to him, and in committee work others might leave him to bear the burden alone, he would simply gird on his armor and do the work; this was not due to an overweening opinion of his abilities, but, having grasped the handles of the plow and satisfied that the labor was honorable and for the betterment of his fellows. He would not allow difficulties to daunt him, nor obstacles to stand in his way, but with his great experience and knowledge of men he would find a way where the less able or courageous man would succumb.

"One of his favorite expressions was, 'I had no business whatever to go into this, but nobody else seems to care to push this so I must go on with it.' He frequently sought advice from those whom he believed could throw light on the problems in which he was engaged, and when discussing suggestions his quick grasp of possibilities was one of the prominent characteristics of his mind.

"His conscientiousness was a marked trait: if he had received a thought or suggestion which seemed to him valuable it was not his habit to appropriate it as his own, but he was glad to give credit to whom credit was due, and if he made a mistake or committed an error in judgment he seemed to take a delight in saying, 'I at one time thought thus and so, but I know better now.'

"Service was the keynote of his life. He had the power of directing others and gathering around him subordinates, but, at the same time, he loved detail, for he realized that many a great work would be ruined by neglect of some important detail which might seem trifling to the inexperienced but was really the key of the situation. He never thought much of his ability to speak and yet his friends, without exception, were glad to have him on their side. As a speaker he was convincing, relying upon righteousness of the cause which he was advocating and believing that all that was necessary to do to win was to state the facts. He well knew the value of a phrase or a witty turn, and he often confused the enemy by a bright sally; his repartee was remarkable and when he and his friend Redsecker were surrounded by congenial spirits, who could appreciate the play of wit, he was at his best. His sense of humor was a saving element, and the relief which it gave him when harassed by carking cares was most effective; but now that he is gone the memory of the great work that he has done in uplifting pharmacy, and his great work in moulding and influencing legislation, his quickness to detect defects in laws bearing upon pharmacy,



and his great influence with legislators made him a power for good, and it will be impossible for any one to take his place in this line of work.

"His religious life was characterized by a simplicity in devotion which was most remarkable. Caring little for the applause of men, a large part of his work was given to quiet deeds of charity and service. Whether it was a man besotted with drink at the Galilee Mission, a little child in his Sunday-school, an aged woman tottering to the grave, or a young man suffering from the effects of sin, his ear was ready and his hand stretched forth to help, because the secret of his life was service to his Master."

*Professor C. B. Lowe* said he was glad Professor Remington had prepared this true and grateful record of Mr. Kline, whose life was so full of usefulness. In many places he would be greatly missed, especially in the Pennsylvania Pharmaceutical Association where he was a tower of strength. In connection with his friend Mr. Redsecker, it was a great treat to listen to their sallies of wit and repartee. He would also be greatly missed in the College, but more especially in church work. He was glad that Mr. Kline showed by his activities in the church that a very busy man in business affairs could also prove to his business, associates and to all others that business activity need not prevent a person being active and useful in the affairs of the church.

*Joseph W. England* said he felt that the highest tribute he could give to Mr. Kline was that he was a strong, broad-gauged Christian gentleman, one who practised what he preached. He loved work and in fact revelled in it. He was enthusiastic in all he did and strove to make each day's work better than the previous one. He had a most keenly developed sense of honor, and this was notable in his labors in assisting to frame the Pure Food and Drug Law. Doctor Wiley had said he owed more to Mr. Kline than any one else in framing that law. His death was tragic, but he had previously said that were it not for the shock to the living he preferred a sudden death. One of his favorite hymns was "Abide with me, fast falls the eventide," and especially the last verse; and his last moments were typical of his faith in these last lines, and in this faith he had his wish.

*Professor Henry Kraemer* said: "While some of us knew Mr. Kline and recognized his activities in this College and in the National Wholesale Druggists' Association, I must confess I was

not prepared for the outpouring of friends to attest to his worth and to show their respect for him, as was seen at the funeral services held November 30. I could not help but feel that as I had not comprehended the magnitude of his labors and had possibly underrated his influence and efforts as attested by the large congregation on that day, possibly there are others here in our midst whose services we should more deeply appreciate and with whom we should more willingly co-operate.

"The College needs every good man it can enlist in its work and for its support. We need to work together as men who are joined in a common cause. I am sure that if we all practised more of the open and manly criticism that characterized Mr. Kline, and were ready to deal fairly and squarely with each issue as though each one were bound by ties of comradeship and friendship, our College would in the future stand on a still higher plane. It would be safe in the keeping of those who remain and those who follow. May we always have the wisdom and the will to do our work in this exemplary way."

*W. A. Rumsey* said that he had known Mr. Kline for a number of years, more particularly because of his work in the Church of the Saviour, of which Mr. Kline was the Accounting Warden and Superintendent of the Sunday-school. He was a great help to the Rector and when the selection of a Superintendent of the Sunday-school was to be made and Mr. Kline was selected for the position the Rector said that no better choice could be made. The church will sadly miss him because he was always striving to do good to others, and the last act in his life was working and planning for the good of others.

*Warren H. Poley* said that Mr. Kline was too truthful a man for his own best interests. When interests conflicted between the wholesale and the retail drug trade his stand was always on the side of truth and honesty even if against his own business interests.

*Edwin M. Boring* said he had known Mr. Kline for over thirty years, and as he listened to the remarks that had been made his heart responded, and he wished to say that he was in full accord with all that had been said.

At this point in the proceedings Professor Remington moved that a committee of three be appointed to draft suitable resolutions and to report at the quarterly meeting of the College on December 27—seconded and agreed to.

*E. Fullerton Cook* said that he would like to say a few words as a representative of the young men. Mr. Kline's labors in behalf of the College House for three years were of very active interest in it and had endeared him to the young men. They felt his influence for good while there and they felt it also in the church. The life he had lived was one not so much to mourn for as lost, as it was to be glad that we had come in contact with it. Its influence was such as to make it a model for us all to pattern after.

*John F. Hancock*, of Baltimore, said he was very sorry he could not get in earlier but there was no train he could take that would permit him to be present at the opening of the meeting. He said that he admired Mr. Kline very much and that he had known him many years, and he had never met any man more poised and reliable. No doubt the eulogies passed on him in this meeting were by men who knew him better. He will be missed by a large circle. He was a great, a good, a useful man, fitted for every position he had been called to fill. These qualities must have been laid in his youth. He made the best use of his opportunities. All these memories should cause us to cherish him, for he was full of energy and devoted to his work. It made one feel proud to know such a man and to have been associated with him. This influence extended more and more like the ripple on the lake. He will continue to live in our memories. Mr. Kline's life connected closely with other great and good men who lived in Philadelphia. Their labors will serve to broaden and extend the work of the College as time goes on, and this will be a cherished memory with me. Others will rise to take Mr. Kline's place, but there will be no duplication of his life. Others will work on and leave to others the work that Mr. Kline and others have carried on for the best interests of pharmacy and the College.

The President in closing the meeting said that he felt that Mr. Hancock had greatly honored the College by his presence and he highly appreciated the sentiments he expressed.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

#### DECEMBER PHARMACEUTICAL MEETING.

The regular pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday, December 21, with Dr. A. W. Miller, Corresponding Secretary, in the chair.

Mr. Stewardson Brown, Curator of the Botanical Section of the

Academy of Natural Sciences, Philadelphia, gave an illustrated lecture on the subject "Botanizing in the Canadian Rockies." Mr. Brown gave an interesting account of a botanizing trip made in the summer of 1908 along with a geographical exploration party. The territory explored was that near the headwaters of the Saskatchewan and Athabasca Rivers, which have their origin in the great Columbia ice-fields. Mr. Brown collected some 3500 specimens, and exhibited beautifully colored lantern slides of the most characteristic and abundant of these, such as *Salix herbacea*, a small plant consisting of three or four leaves and catkins, which is the most abundant plant above the timber line, growing at an elevation of 7000 or 8000 feet; species of primrose; species of pulsatilla, including *Pulsatilla occidentalis*, found in bloom on the edge of a snow bank; species of saxifrage, orchid, etc.

Remarks on Mr. Brown's address were made by the Chairman, and Professors Remington, Kraemer, and LaWall, the latter of whom moved a special vote of thanks to Mr. Brown, which was unanimously adopted.

A paper entitled "The Practical Application of the Twitchell Process of Fat Decomposition and Recovery of Glycerin," by W. J. Warner, of Los Angeles, Cal., was read on behalf of the author by Professor LaWall.

A resolution pertaining to pharmacopœial revision offered by M. I. Wilbert at the previous meeting and laid on the table for further consideration (AM. JOUR. PHARM., December, 1909, vol. 81, p. 593) was read by Professor Kraemer, and on motion of Professor Remington adopted as published.

Professor Kraemer spoke of the work being done by Dr. Joseph Neff, Director of the Department of Health of Philadelphia, to protect the health of the citizens, and after discussion offered the following resolution, which was adopted:

We, the members of the Philadelphia College of Pharmacy assembled at this meeting, desire to place on record a statement that the attitude taken by the Director of the Department of Public Health of Philadelphia is in accord with the principles of the members, and that we heartily endorse his efforts for the suppression of nostrums of all kinds used or advertised as being of use in the treatment of diphtheria, or other infectious diseases, and further that we also heartily endorse his efforts to enlighten the public in preventing disease and promoting the health of this community.

FLORENCE YAPLE,  
Secretary *pro tem*.



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## PHARMACOGNOSY AND THE UNITED STATES PHARMACOPŒIA.\*

BY HENRY KRAEMER.

Pharmacognosy in both the modern acceptation and application of the term is a comparatively new department of science, although the history of the use of vegetable drugs is as old as that of medicine itself. While we have been accustomed to look upon pharmacognosy as a division of botany, it has so expanded within the past twenty-five years as properly to be regarded as a distinct branch of science. As in bacteriology the problems in the study of bacteria are different from those of the botanist, so in pharmacognosy the problems differ from those in pure botany, being on the one hand similar to those which are considered by the modern agriculturist. In other words, pharmacognosy involves not only a study of botany, including morphology and anatomy, but also studies in chemistry, including both plant chemistry (phyto-chemistry) and drug chemistry (pharmaco-chemistry). The pharmacognosist is not merely concerned with the dried drug as he sees it, but also with those conditions which influence the development of the constituents of the plant or which modify those constituents in the drug on which medicinal activity depends. Indeed the subject is a very broad one and a very complicated one when viewed from all sides, and it is a long way from the living plant from which the drug is derived to the laboratory of the pharmacist who makes the preparation. There

\* Read before the City of Washington Branch of the American Pharmaceutical Association, January 5, 1910.

are problems at every point in the oftentimes circuitous route which the drug travels before reaching its final destination in the finished preparation. In addition to the field problems, as those involving the determination of the identity of the plants and variation in the constituents at different seasons of the year, there are also other factors of which cognizance must be taken that influence the quality and appearance of vegetable drugs, as the degree of skill used in the drying and curing of the drugs; the proportion of other plant parts, as of stems attached to roots; the manner and length of time of keeping; and attacks of fungi and insects, etc. We may say, therefore, that pharmacognosy begins with the study of the plants yielding vegetable drugs and ends with the determination not alone of their identity but of their quality also.

When one considers that about 70 per cent. of the articles included in the Pharmacopœia are vegetable drugs, their constituents, or their preparations, it is seen that the users of the Pharmacopœia must have a knowledge of pharmacognosy, and that the physician is directly dependent upon the work of the pharmacognosist for the therapeutic efficiency of many of the most important medicines which he prescribes. It matters not how perfect the methods for making preparations are if the materials used in their preparation are spurious, worthless, or vary in quality to a considerable extent. There is no doubt that many useful drugs and their preparations have become and are becoming obsolete for the reason that other drugs which are inert or have different properties have been or are being substituted for them. Such a condition not only baffles the efforts of the therapist but also tends to deprive him of remedies which heretofore were considered to have certain valuable properties. But some will say that the drugs are becoming scarce. This is true in some instances, but instead of simplifying the question, renders it more complicated in that the necessity arises for detecting the spurious substitutes that are frequently admixed with the genuine drug or even entirely replace it.

#### THE U. S. PHARMACOPŒIA.

While it is not possible to consider all the various phases of pharmacognosy in the Pharmacopœia, it is desirable to give definitions and descriptions of the official vegetable drugs which are adequate for the establishment of their identity and efficiency. In other words, it is the results of the studies in applied pharmacog-

nosy which should be included in the Pharmacopœia, leaving the problems and studies in pure pharmacognosy for the text-books and reference books.

That part of the U. S. Pharmacopœia VIII devoted to pharmacognosy is not only not abreast with the other departments of this work, but, furthermore, when this part is compared with that in the foreign pharmacopœias it is found to be lacking in important particulars. This would lead to the conclusion that we in this country not only do not recognize the importance of the subject but that we are more or less indifferent to the nature of the drugs which we employ. That this condition, or worse, still prevails, is shown by the expressed desire to eliminate standards for crude drugs. It has been proposed to permit all grades of crude drugs to be admitted to this country and to be sold and used in the making of galenicals, the only provision suggested being that the finished preparations shall be standardized. Apart from the many objections that can be raised against such a procedure, as, for example, the inadequacy of the assay processes themselves to confirm the identity of the drug on the one hand or its full medicinal value on the other, there are other practical difficulties in the way. To illustrate, Dr. J. M. Francis states in commenting on the results of his assay of many thousands of pounds of belladonna root of the market, that, "While theoretically an increased quantity of poor drug will make a good fluidextract, if the latter be standardized by assay, there are, however, practical objections to using an excessive quantity of drug, as the fluid will be highly charged with extractive matter and will not keep well."

On the face of it, it is not reasonable to suppose or believe that a good fluidextract or tincture can be made from a poor drug any more than to suppose that good malt can be prepared from barley grains of poor quality or a good extract of beef from meat of poor quality. It is true that a certain amount of alkaloid may be extracted in some instances from a mouldy, wormy, or otherwise inferior drug, but no one would contend that in the majority of cases the medicinal properties of a tincture, fluidextract, or infusion are wholly dependent upon the percentage of one such principle alone or that the preparations would be as good in other respects as those made from drugs of good quality. If, however, this be contended, then the better procedure would be to use the alkaloids and other isolated principles themselves. Discussing this question in a recent

paper Tschirch<sup>1</sup> writes: "For when the isolated substances are tested pharmacologically, it becomes evident that their action does not correspond with that of the drug itself—for the latter scarcely ever contains a single active constituent but frequently a remarkable mixture of substances that are often antagonistic in their effects. I will refer only to rhubarb, which, in addition to laxative anthraglucosides, contains astringent tannoglucosides, and owes its therapeutical use to the simultaneous occurrence of these two antagonistic groups of substances. Although, unable to free ourselves from the views of Galen, drugs are still called 'simples,' they are in reality far from simple; indeed they are extraordinarily complex substances."

Again, Turner in a recent paper<sup>2</sup> has called attention to some of the newer views in regard to the components of drugs on which medicinal activity depends and to a tendency to abandon the idea that the principles separated by assay truly represent the value of the drug. He says: "Boulanger-Dausse in *Bulletin des Sciences Pharm.*, No. 1, 1908, pays particular attention to this question and comes to the following conclusions:

"The endeavor to isolate the 'alkaloid' to which scientific pharmacy paid such vivid attention for nearly one hundred years begins to lose its practical significance. The chemistry of colloids partly takes its place and the chemist and pharmacologist pay more and more attention to certain complex ingredients of drugs, or, as they are usually called, 'extractives' of drugs.

"A diligent and successful investigation of certain drugs showed conclusively that the active principles isolated from them in the course of one hundred years and studied both chemically and pharmacologically did not satisfy the requirements which the physician had right to put to them. Cinchona, digitalis, ergot, rhubarb, buckthorn, cascara sagrada, kola, opium and nux vomica are the best examples illustrating what was said before.

"Many prominent pharmaceutic chemists and, lately, especially Kunz-Krause, recognized this in proper time and showed that in many cases the production of chemically pure active principles of drugs can no longer be the ultimate purpose of pharmacy. It is more proper to expect that in the future pharmaceutical science will direct its work toward production of chemically unchanged colloidal

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<sup>1</sup> *Pharm. Jour.* (London), 83, 420, October, 1909.

<sup>2</sup> *AM. JOUR. PHARM.*, 81, 125, March, 1909.



drug preparations which will have the *total* action of the respective drug."

At any rate, we have not advanced to that point where we know or can isolate the active constituents in all cases, or where we are willing to say in those cases where certain active constituents have been isolated that they represent the full medicinal value of the drug and could replace the preparations. Hence it cannot be gainsaid that there is an urgent demand for accurate and adequate, if not full, pharmacognostic descriptions in the Pharmacopœia. With the introduction of standards for crude drugs which not only fix the percentage of certain active constituents but which assure their quality in other ways, preparations can be made by the pharmacist on which the physician can rely for their therapeutic efficiency.

It is not too much to claim that with every drug it is possible to indicate by adequate descriptions and if necessary by other tests than assays a standard quality which will insure uniformity, stability, and efficiency of the preparations into which the drug enters. If there is any class of articles included in the Pharmacopœia which requires a purity rubric it is the vegetable drugs, as they vary in medicinal activity from practically zero up to 99 per cent., the official drugs being in some instances entirely substituted by other drugs, or they are of varying degree of quality because of their age, or the conditions under which they have been kept, or because of the presence of a large excess of other parts of the plant than that designated as the drug, or because of foreign impurities. It would seem to be unnecessary to refer to this subject, as the principle is one so self-evident and fundamental to the observing pharmacist, as well as critical practitioner, who is studying the effects of drugs and their preparations on his patients. The manufacturers of specialties understand this, as do also some of the large manufacturing houses, and this is no doubt one of the reasons why their preparations are specified and will continue to be used by those physicians who are not trusting to luck or chance.

#### FOREIGN PHARMACOPŒIAS.

The importance of adequate pharmacognostic descriptions and tests appears to be recognized by the compilers of all the more recent foreign pharmacopœias that have come to my notice. The question with the revisers of these books seems to be not a matter of considering the pharmacist's ability or inability to apply the

required tests and use the knowledge given, but primarily to include such descriptions and tests as will insure the quality and genuineness of the articles both under vegetable drugs and medicinal chemicals. One does not go very far in the examination of these books without getting the idea that the pharmacist is expected to have the necessary books of reference, the apparatus, and the training which will enable him to use the pharmacopœia in determining the character of the products therein given. While some of these pharmacopœias do not include tests requiring special expensive pieces of apparatus as is required in our own Pharmacopœia, as in the tests involving the use of the polariscope, they all require the use of the microscope. In other words, the foreign pharmacopœias are more balanced in their treatment of the various subjects, and we would not be likely to hear the comment on a foreign pharmacopœia, as we have regarding our own standard, that it is a "chemist's book."

The treatment of vegetable drugs in the foreign pharmacopœias may be quite complete, as in the Netherlands Pharmacopœia, where a page or more is frequently given to each drug. Or it may be what would be termed adequate, the intention being that the user shall be familiar with the structure of the typical drug either from the study of the drug itself or the books of reference, as in the Swiss Pharmacopœia, the French Codex, the Pharmacopœia of Japan, and others. Besides, in a number of foreign pharmacopœias various constants are given, including percentage of ash, percentage of extractive, as also various special tests, some of these being micro-chemical. Generally speaking, the treatment of the microscopic structure is an essential feature of the descriptions, and may be of the crude drug alone, or more especially of the powdered or ground drug, or of both. In some of these pharmacopœias powdered drugs are not recognized or only occasionally referred to, probably from a recognition of the difficulty of identifying and determining the percentage of impurity or admixture, and also perhaps in view of the fact that very many drugs deteriorate or lose certain desirable properties when in the comminuted condition. As one goes through these pharmacopœias he is impressed by the fact that there are standards for vegetable drugs as there are for medicinal chemicals and the adequate descriptions and special tests correspond to the identity tests given for chemicals, and the revisers have availed themselves of the scientific progress that has been made in all lines touching their own work.

PHARMACOGNOSY AND COMMERCIAL DRUGS.

It appears to me to be unfortunate that the Committee on Drug Market of the A. Ph. A., representing as it does an association composed of the leaders in education and the scientific workers in pharmacy in this country, should have presented at the last annual meeting a report which tends to throw discredit upon practical or applied pharmacognosy in this country. This is the more to be deplored because of the fact that the Committee on Drug Market of the National Wholesale Druggists' Association incorporated the findings of the A. Ph. A. committee in its report presented at the Richmond meeting and also because the report has been commented upon and considered to represent an actual condition. The N. W. D. A. Committee cannot of course be blamed for accepting the findings of a committee of our leading scientific association. While I do not know who the experts were to whom specimens were submitted by the A. Ph. A. committee, I may say that I have in mind a recent graduate of a college of pharmacy who was able to take a drug like the one reported on by the A. Ph. A. committee and quantitatively separate the component drugs of the mixture. I do not mean to imply that this is a piece of off-hand work, but that it requires a certain amount of knowledge, training, and some patience; but on the other hand I do want to state that any one claiming to be trained in applied pharmacognosy should be able readily to make a differentiation of the component drugs of such a mixture as is referred to in the report of the committee of the A. Ph. A., and, furthermore, that the condition of the drug market creates the necessity for work of this kind. As a matter of fact, questions of this kind arise daily in the drug market, and it behooves us to frame the Pharmacopœia in such a manner as to make it a valuable aid and guide in this practical and all-important work, and warrants us in looking to the colleges of pharmacy to train their students in such a manner as to enable them to be useful in this particular field.

Such a report as that of the A. Ph. A. committee tends to hinder progress in that it leads importers and dealers to think that there is no way out of their difficulties, and, what is still more deplorable, leads those who engage in fraudulent practices to feel that there are probabilities that their practices will not be detected. Again, such reports tend to minimize the importance of the question in the eyes of dealers, and finally to cause delays in the progress of the sciences of both pharmacy and medicine.

However, we have a responsibility in these matters which we cannot evade, and the dealers in drugs look to us to study the conditions and the materials, and to furnish descriptions and tests for determining identity and establishing standards of quality which will be of practical assistance and which they can rely upon with as much certainty as their tests and standards for chemicals. There appears to me to be no reason why the whole subject of the purchase and sale of vegetable drugs should not at least be on as satisfactory a basis as that of spices. I have sufficient faith to believe that when the standards and tests for vegetable drugs are developed as they should be, or adopted even as we know them to-day, there will be no more quibbling about the difficulties of obtaining vegetable drugs of satisfactory quality than there is about medicinal chemicals at the present time, and that the dealers will be glad for the adoption of such standards. With the establishment of fair standards it will be possible for importers and wholesale dealers to insist that the garbling of drugs and the removal of extraneous matter shall be carried on by the collectors and distributors before they enter commerce. Such a procedure would be wholly in accordance with the modern way of handling problems of this kind. Why shall 40,000 druggists be worried about gross adulterations and admixtures when these can for the most part be detected at the point where the drugs enter commerce and where such pressure can be brought to bear upon the collectors abroad as well as in this country as will cause them to remedy deficiencies in their knowledge of the drugs or plants from which they are derived and prevent continued carelessness in their collection. I am satisfied that the lack of uniformity in the preparations of vegetable drugs at the present time, as shown both by chemical and pharmacological assay, is due to various factors not connected with plant growth, rather than to inherent variation in the drugs themselves, which usually only vary within certain narrow limits.

#### U. S. PHARMACOPŒIA IX.

It has been pointed out that in the commerce of drugs practical problems are continually arising, and hence the Pharmacopœia should contain such information as will help in the solution of these problems. That part of the U. S. Pharmacopœia devoted to pharmacognosy has not had a thorough revision since at least 1890, and with the progress that has been made in applied pharmacognosy



in that time, the necessity arises for a vast amount of work in bringing this part up to date and in making it a guide and standard for practical purposes.

In a previous paper<sup>3</sup> I pointed out some of the difficulties connected with revision work, particularly in this department. Soon after the Subcommittee on Pharmacognosy of the last revision began its work it became evident that it was not a question of developing the special work in hand or improving the Pharmacopœia, as it was of conducting a campaign of education showing the necessity for and importance of the work. While it remains to be seen what has been accomplished by this campaign of education, there can be no question as to what is required in the inspection and selection of drugs.

In order that the U. S. Pharmacopœia IX may not only be abreast of the times but also be a valuable guide and handbook, and at the same time a credit to the revisers as well as a source of pride to the physicians and pharmacists of this country, it is important in the first place that the Pharmacopœial Convention abstain from passing any resolutions which would tend to bind the hands of the Subcommittee on Pharmacognosy and prevent them from doing their best work. Tentative recommendations might be made by the Convention and referred to the subcommittee for their consideration and final decision, and these should be welcomed.

This leads me to say that the work of a subcommittee may not only be handicapped by binding resolutions adopted by the Convention but also by the giving of instructions by the Committee of Revision which tend to hinder the work. Here it may be pointed out that the Committee of Revision as a whole does not appear to me to be so constituted as to be any more capable of making binding recommendations on special subjects than the Convention itself. Therefore it is to be hoped that in the work of the next revision the subcommittees will be free to carry on the work to the best of their knowledge, experience, and ability, and for which they will be held responsible. In my previous paper, to which reference has already been made, I have discussed this matter at some length, and it will not be necessary to go into it further at this time. But after all, as I have elsewhere<sup>4</sup> stated, "it is not so much a matter of

<sup>3</sup> AM. JOUR. PHARM., 80, 81, February, 1908.

<sup>4</sup> *Am. Dr.*, 55, 378, 1909.

method as it is of selecting men to carry on the work of revision who comprehend the scope and intent of a pharmacopœia," for even with the most perfect system there is yet a possibility that the best will not be attained.

In view of the large amount of work which the Subcommittee on Pharmacognosy will have to do in the next revision this committee should be increased and empowered to employ assistance for carrying on certain detail work. Of the subjects to which special consideration should be given, the following may be mentioned: the definitions both in relation to commercial varieties and botanic species, with the object of making them more exact and at the same time more easily understood; the microscopic structure of the drugs, with the view of aiding identification; special tests and standards for assisting in the determination of quality; and finally the question of the inclusion of powdered drugs with adequate descriptions and tests. In order to carry on this work in a thorough manner it is desirable that the Subcommittee on Pharmacognosy be closely allied with the Bureau of Plant Industry and the Botanical Society of America. Again, it is desirable that this committee be in close touch with the large crude drug dealers and importers, for they could undoubtedly supply much information that cannot be gotten in any other way and would be in a position to procure material for the use of the committee. Furthermore, the Subcommittee on Assays should co-operate very closely with the Subcommittee on Pharmacognosy, and the latter should not only furnish the drugs to be assayed but provide, where possible, microscopical or other suitable tests for the identity of the proximate principles obtained in the assays.

But already I hear objections to the development of this work along modern lines. The first is that if there is an increase in the number of vegetable drugs or an extension of the space devoted to their consideration, the Pharmacopœia will be less popular with physicians. To this I merely wish to reply that I have reason to believe that the work will be more popular with physicians in that they will be assured of greater uniformity and efficiency in the official preparations.

The other objection that will be brought forward is that the pharmacist will not be able to apply the information given. While this may be true to a certain extent, it is not an objection which should be allowed to hinder progress, and it is one which is met in

part abroad by the colleges of pharmacy providing special courses of instruction for pharmacists following each revision of the Pharmacopœia. But if the colleges do their part it is only a question of time when this objection can be eliminated entirely.

#### CONCLUSIONS.

In this paper I have attempted to show that pharmacognosy is a science of fundamental importance to the pharmacist, and that the results of the studies in pharmacognosy are of the greatest value to the physician in assuring him uniform and efficient medicines.

I have called attention to the fact that the foreign pharmacopœias give more uniform consideration to the various subjects and are as strong in their treatment of pharmacognosy as is that of chemistry and pharmacy.

It was pointed out that the pharmacognosy of the U. S. Pharmacopœia has not been thoroughly revised for a decade or more, and that the existing needs demand that it shall be completely modernized. Some of the features that should be considered have been enumerated. The work before the next Subcommittee on Pharmacognosy will be an extensive one, and a wide co-operation is desirable.

Finally, it may be again pointed out that the colleges and schools of pharmacy have a certain share and responsibility in this work. Therefore their courses should in part be based upon the Pharmacopœia and should be such as to forestall the assertion that pharmacists will not be able to use the Pharmacopœia when improved to the extent that existing conditions demand and by virtue of which it should alone exist.

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#### THE BASIC PRINCIPLES OF PHARMACOPŒIA REVISION.

BY H. H. RUSBY, M.D.

A careful reading of the papers by Messrs. Wilbert and Remington in the December number of the AMERICAN JOURNAL OF PHARMACY prompts a few words of comment concerning the basic principles on which revision should proceed.

Mr. Wilbert's able handling of those principles which he has considered cannot be criticized, though Prof. Remington has

pointed out in good time some serious misstatements of fact. Mr. Wilbert's serious error has been his complete omission of reference to other principles of far more importance than those which he has considered. It is of great importance, as he has pointed out, that physicians' views as to articles which they desire to have recognized in the Pharmacopœia should receive the closest attention, and should be met as far as possible, but it is of equal importance that the pharmacists should have standards of identity and purity for the articles which they are compelled to supply, on demand, without any regard to the views of physicians as to whether that demand is judicious. It is of even greater importance that the administrators of Federal and State laws should have standards for the identity and purity of drugs and medicines commonly imported and used, without any regard whatever to the views of physicians as to the therapeutical merits of those articles. The physicians' duty is to educate the members of their profession as to the proper articles to employ. They have innumerable text-books for this purpose, and they, and not the Pharmacopœia, constitute the medium that should be employed in that educational work. The Pharmacopœia is in no sense a text-book. If physicians have neglected their duty, or failed in its performance, they should correct themselves. Mr. Wilbert calls for a book that will "command the respect and admiration of physicians." They now have more such books than they can use, but the Pharmacopœia was never designed as an object of admiration, however well it might be if it could be admired. It is a working standard, and it should go wherever there is work to do. Moreover, it is a legal instrument and that alone debars it from being made the subject of class legislation. Finally, after all has been said as to what it should be, it may be pointed out that its own fate depends upon its meeting the requirements above referred to. If it should be converted by the committee into a text-book for the sole use of physicians, and only of those of a certain class, it will be at once relegated to that position, will cease to be an official work, and will be superseded by one constructed on the only plan that can fit it for the work for which a national Pharmacopœia is intended, and for the use of other classes who far outnumber the physicians.



## THE PURITY RUBRIC AND THE U.S.P. TESTS.\*

With Notes on Quantitative Methods for Certain Pharmacopœial Compounds.

BY ATHERTON SEIDELL AND M. I. WILBERT.

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As has been repeatedly pointed out, the Federal and States Pure Food and Drug laws have given to the Pharmacopœia of the United States an entirely different standing from that occupied by it at the time that the present official revision was authorized by the Pharmacopœial Convention, which met in May, 1900, and it is also well known that the Pharmacopœial Convention which is to be held in the City of Washington in May, 1910, will meet, as a legally chartered organization, under entirely different conditions from those prevailing at any one of the previous nine conventions. The responsibilities assumed by the delegates attending this convention are therefore such that they and all others who are in any way interested in the scope and content of the Pharmacopœia of the United States should thoroughly inform themselves beforehand on the general principles that will come up for discussion.

From the point of view of the chemist, no one feature of the prospective revision of the Pharmacopœia is of greater importance than the establishment of reasonable standards of strength and purity, and the co-relating of the several tests and assays with the requirements under what has become known as the purity rubric.

Our Chairman, in his recent circular letter, calls renewed attention to the fact that, "in many cases the Pharmacopœia requires that its products shall be of a definite strength or purity without supplying the method to secure such results."

It is also well known that while many of the chemical tests in the U.S.P. are described in detail, others are but briefly outlined, and in connection with some the language used is ambiguous even to the trained chemist and certainly meaningless or misleading to those of limited experience.

Many, if not all of you, will agree with the dictum that if the Pharmacopœia of the United States is to serve, as it really should,

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\* Read at the Division of Pharmaceutical Chemistry of the American Chemical Society, December, 1909.

as the standard for purity and strength of the medicines enumerated in its pages, the requirements should be attainable and the tests necessary to establish the identity, strength, and purity of these medicinal substances should be such as can be followed by all of the directly responsible persons engaged in the medicine supply business.

In other words, given a reasonable standard for a substance, the identity, purity, and activity of this compound should be controlled and guaranteed by each person handling it. It follows, therefore, that the passage from the producer to the consumer should be safeguarded from cupidity and ignorance in such a way that at no point will there be opportunity for deterioration or sophistication without at least a fair chance of the shortcomings being detected before the medicine reaches the consumer.

A prescribed purity rubric which is not accompanied by a clearly described analytical method gives an opportunity for differences in the results which may be obtained by even the most careful analysis working with different methods. As a general principle it would, therefore, appear that in so far as it is possible quantitative analytical methods be selected for all substances of the Pharmacopœia for which a purity rubric is given. Furthermore, it is desirable that, other things being equal, the method applicable to the largest number of compounds containing a given constituent should be selected. Such general methods could then be described at some length in the Appendix, and simply referred to under the description of the compound, in much the same way as the now official titrimetric processes are referred to in the U.S.P.

As a practical demonstration of the possibility of elaborating such efficient yet simple quantitative methods, the following laboratory notes on some of the Pharmacopœial compounds examined in the Division of Pharmacology of the Hygienic Laboratory during the past year are herewith presented.

*Red Mercuric Iodide.*—The Pharmacopœial purity rubric for this salt requires that it contain not less than 98.5 per cent. of pure mercuric iodide. Tests for the identity and for the presence of certain impurities are given by the Pharmacopœia but no quantitative method by which the required purity may be determined. There are a number of processes which probably could be adapted to the present purpose, but the one which has been found most satisfactory is as follows:

A weighed quantity of the sample (about 1.0 Gm.) is mixed

with about 50 c.c. of  $\text{H}_2\text{O}$ , 5 Gms.  $\text{KOH}$ , and 10 to 20 c.c. of 3 per cent. solution of hydrogen dioxide; the solution warmed gently until the decomposition of the mercuric iodide is complete.<sup>1</sup> The gray mercury residue is filtered on a weighed porcelain Gooch crucible, washed with cold  $\text{H}_2\text{O}$ , dried at about  $60^\circ$  and weighed.  $\text{Hg} \times 2.2692 = \text{HgI}_2$ . For the iodide, the filtrate from the mercury is evaporated to about 50 c.c., cooled and filtered into a glass stoppered bottle; about twice its volume of concentrated  $\text{HCl}$  and 10 c.c. of chloroform are added. The mixture is then titrated to disappearance of the pink color of the chloroform with 0.1 N  $\text{KIO}_3$  solution.<sup>2</sup> The potassium iodate solution may be conveniently standardized against pure potassium iodide. Duplicate determinations upon a sample of red mercuric iodide gave the following results:

	Sample	Wt. of Gooch 1st.	Crucible 2nd.	Gm. Hg.	Calc. % $\text{HgI}_2$ .	C.c. 0.1 N $\text{KIO}_3$ Sol.	Calc. % $\text{HgI}_2$ .
[a]	1.0 Gm.	8.1786	8.6152	0.4366	99.1	43.7	99.2
[b]	1.0 Gm.	7.1758	7.6143	0.4385	99.5	43.7	99.2

The process as here outlined is rapid enough for all ordinary purposes. Only one weighed portion of the sample is required for the determination of both constituents, and the method will no doubt yield concordant results in the hands of different analysts.

*Potassium Iodide.*—The quantitative method given by the Pharmacopœia for this salt is the usual argentometric titration which, of course, does not differentiate between the several halogens. The titration with standard potassium iodate as outlined above offers certain advantages over the use of silver nitrate, which more detailed experiments will no doubt demonstrate. It is to be noted in connection with the iodate titration that the end point of the reaction is to be taken at the disappearance of the pink color of the chloroform indicator without reference to the pale yellow color of the aqueous layer which persists.

*Tincture of Iodine.*—The titration of a 5 c.c. portion of tincture of iodine as prescribed by the Pharmacopœia gives rise to somewhat variable results due to inaccuracies in correctly measuring this relatively small volume of the sample. The quantity of iodine calculated from several duplicate titrations may vary by as much as 0.3 Gm. The use of aliquot portions of the sample after dilution

<sup>1</sup> M. Kohn, *Z. anorg. chem.*, **59**, 108-10; *Chem. Abstracts*, **2**, 2911.

<sup>2</sup> L. W. Andrews, *J. Am. Chem. Soc.*, **25**, 756, 1903.

would, of course, obviate this difficulty. Although no determination of the potassium iodide in tincture of iodine is prescribed by the Pharmacopœia, a definite amount of this ingredient is specified by the formula. It therefore appears that a quantitative test for potassium iodide might well be included. A satisfactory method for this determination is as follows: 25 c.c. of the sample are evaporated to dryness in a dish and the free iodine removed by volatilization. The residue after being heated to dull redness is dissolved in water, the solution filtered and diluted to 100 c.c.; 25 c.c. of the latter are then placed in a glass stoppered bottle with 50 c.c. of conc. HCl and 10 c.c. of chloroform and titrated to disappearance of pink color of the chloroform with 0.1 N KIO<sub>3</sub> solution. Several determinations upon two samples of tincture of iodine gave the following results:

Sample No.	C.c. used	Wt. of Platinum Dish		Residue	C.c.o. KIO <sub>3</sub> for $\frac{1}{2}$ residue		Gm. KI per 100 c.c. tinctures
		empty	and residue		Gm. KI		
234	25	31.8809	33.1160	1.2351	18.6 = 0.3089		4.94
229	25	31.8915	32.9640	1.0725	16.0 = 0.2656		4.25
229	25	31.8855	32.9747	1.0892	16.3 = 0.2706		4.32

The preceding results indicate that this iodate titration method can probably be applied with success to many of the iodine compounds of the Pharmacopœia for which quantitative methods are at present not given. It may also be expected that the determination of mercury in many of its salts can be satisfactorily accomplished by a modification for the method described above for red mercuric iodide.

*Lead Acetate.*—The purity rubric of the U.S.P. requires that this product should contain not less than 99.5 per cent. of  $\text{Pb}(\text{CH}_3\text{COO})_2 + 3\text{H}_2\text{O}$ , since, however, no quantitative method is prescribed by which this limit of purity may be determined, the following plan was applied to two samples of the salt with satisfactory results: A weighed sample was dissolved in about 50 c.c. of water and a slight excess of dilute  $\text{H}_2\text{SO}_4$  added. The precipitated lead sulphate was filtered on a weighed Gooch crucible, heated gently over a Bunsen flame, cooled, and weighed. The results were as follows:

Sample No.	Gms. used	Wt. of Gooch crucible		Wt. of PbSO <sub>4</sub>	Calc. % $\text{Pb}(\text{CH}_3\text{COO})_2 + 3\text{H}_2\text{O}$
		Alone	+ PbSO <sub>4</sub>		
207	0.5	7.1533	7.5706	0.4173	104.3
226	0.5	8.3308	8.7368	0.4060	101.6



Both of the above samples and indeed a number of others failed to give a clear or only slightly opalescent solution when dissolved (1 in 10) in recently boiled water. It is therefore questionable whether this test for limit of carbonate is a satisfactory criterion for judging the quality of lead acetate samples. The gravimetric determination as above outlined shows conclusively that the samples have either lost water of crystallization or, as is more probable, are contaminated with the basic salt.

*Acetanilide.*—A rapid procedure for the quantitative analysis of this compound is the bromate titration method proposed by one of us in 1907.<sup>3</sup> A standard bromate solution which may be the Koppeschaar's solution of the Pharmacopœia is required. The weighed sample of acetanilide is dissolved in about 50 c.c. of a mixture of one part concentrated HCl and 2–3 parts water, the solution boiled for five minutes and titrated to the appearance of pale-yellow color with standard bromate solution, 1 c.c. 0.2 N bromate solution being equivalent to 0.004504 Gm. acetanilide. The following results were recently obtained upon a sample of acetanilide, m. pt. 112°–113°:

Weighing Bottle and Sample		Sample	Am't used for titration	C c. 0.2 N KBrO <sub>3</sub> sol. required	Calc. % acetanilide
1st. Wt.	2nd. Wt.				
14.0581	13.6807	0.3774	all	84.2	100.5
13.6807	13.1282	0.5525	½	61.5	100.2
13.1282	12.5965	0.5317	¼	29.7	100.7

*Ammonium Benzoate* and other Ammonium Salts.—As has been shown in another paper<sup>4</sup> (Seidell and Menge), a simplified distillation method is well adapted to the analysis of ammonium benzoate samples, and the formaldehyde titration method of Schiff and other investigators is applicable to practically all other ammonium salts for which the Pharmacopœia gives a purity rubric but no quantitative method of analysis.

As an illustration of Pharmacopœial tests that appear to require some additional elaboration it will suffice to call attention to the following:

*Sodium Benzoate.*—The quantitative test for this salt as prescribed by the Pharmacopœia requires that the sample be ignited at red heat and the aqueous solution of the residue be titrated with

<sup>3</sup> Seidell, *J. Am. Chem. Soc.*, 29, 1091, 1907.

<sup>4</sup> This JOURNAL, 82, 12.

0.5 N HCl, using methyl orange as indicator. The experience in this laboratory has shown that even in spite of the greatest care the unburned carbon left after the extraction of the incinerated residue retains an appreciable amount of alkali, and therefore in order to obtain satisfactory results it is necessary to make a second ignition of this unburned and extracted carbon, and add the solution of the second residue to that of the first, before making the titration for the total alkali. The modified procedure may be conveniently carried out as follows:

The weighed sample is ignited thoroughly in a platinum dish, the residue extracted with hot water, and the solution filtered through an ashless filter, the unburned carbon washed several times, and then returned together with the filter paper to the platinum dish and ignited. The second residue is dissolved in water and added to the filtered extract of the first residue and the solution titrated with 0.5 N HCl. The following typical results indicate the necessity of the above modification:

Sample No.	Wt. used Gm.	C.c. 0.5 N HCl required,		Calculated $C_6H_5COONa$ .	
		1st Extract.	2d Extract.	U. S. P.	Modified.
232	1.0	13.15	0.35	94.7	97.4
232	1.0	12.7	0.85	91.5	97.6
232	1.0	12.9	0.5	92.9	96.5
232	1.0	12.6	0.8	90.7	96.5

A number of samples of sodium benzoate from several sources have been examined by the above modified method, but none contained the 99 per cent. pure sodium benzoate required by the purity rubric of the Pharmacopœia. It must be mentioned that the experimental error in the determination could be reduced considerably by either the use of a larger sample or of a more dilute standard acid. With the present quantities, an error of 0.1 c.c. of the standard acid corresponds to about 1.0 per cent. of the salt.

As indicated above, we believe that the foregoing notes serve to illustrate the possibility of adapting more or less well-known quantitative methods of analysis to the examination of Pharmacopœial compounds. Such simple and accurate quantitative methods together with qualitative tests for impurities of a serious character will give a ready means for controlling the purity rubric of the Pharmacopœia, and raise this requirement to the degree of importance that it deserves.

## PEROXIDE OF HYDROGEN.

BY A. R. L. DOHME, PH.D., AND H. ENGELHARDT, PH.D.

Some months ago an article by Dr. Francis appeared dealing with the preserving of solutions of peroxide of hydrogen by the addition of a comparatively small amount of acetanilide. As nearly as the writers remember, it was stated there that the solutions kept well for more than a year, and that a deterioration did not take place after eleven months, as stated by Professor Coblentz. We have had opportunity frequently to examine samples of peroxide of hydrogen preserved with acetanilide from different manufacturers, and in most cases we found that the preparation smelled strongly of nitrobenzene, showing that a decomposition had taken place. Unfortunately we were not able to learn the age of the preparations. If such a decomposition of the preserving agent takes place, the value of the addition of such material should be seriously questioned. A process of W. Heinrici which is covered by the American Patent 825 883 to preserve peroxide of hydrogen solutions depends on the addition of amino derivatives. Acetanilide, which belongs to this class of compounds, is used in this country only, while in Europe the preserving of peroxide of hydrogen is effected by other chemicals.

Among the preservatives used, the following may be named: Renault and Lepinois recommend the addition of boric acid. Allain recommends the addition of about 1 per cent. of sodium chloride, magnesium chloride, or calcium chloride. According to L. Martin, an addition of 0.5 per cent. of borax preserves the peroxide of hydrogen satisfactorily, rendering it at the same time slightly acid without decreasing the titre of the preparation. From many sides, the addition of an excess of acid has been recommended, since this addition both preserves the peroxide of hydrogen solution and neutralizes the alkalinity of the glass. The fact that acid exerts a good preserving power on the peroxide of hydrogen seems to be acknowledged by most of the manufacturers, because we found recently that samples of nearly all the leading makes of peroxide solution prepared in this country (about six in all) of which some had been preserved by the addition of acetanilide, showed on examination an acidity exceeding that allowed by the U.S.P. If in future the use of acetanilide for preserving peroxide solutions should be prohibited, as it should in our opinion, we strongly recommend the use of an

excess of either sulphuric acid or phosphoric acid, inasmuch as these two acids are not liable to be acted upon by the peroxide. The use of hydrochloric acid or chlorides might lead to the formation of decomposition products which might render the peroxide injurious. The amount of the excess of free acid should in our opinion also be increased above what the U.S.P. now allows, say about double the present amount, as the present official amount is soon reduced sufficiently by the alkalinity of glass containers and the shaking experienced in transit to distant sections to bring it below the safety point, resulting in decomposition and blown corks very frequently. No make that we examined only a few weeks ago contained as little acid as the U.S.P. allows; all of them contained more and the most of them considerably more, though of course in no instance enough to interfere with the usefulness of the product or to cause any irritation when used in wounds or any other sensitive surfaces. If free acid in sufficient quantity will fully preserve peroxide of hydrogen and at the same time in no wise interfere with its usefulness as a remedial or prophylactic agent, surely this is the simplest way to preserve it—but this will of course have to be shown and proven by experiments. In our opinion the value and desirability of acetanilide as a preservative for peroxide solutions is open to question.

In No. 45 of the *Schweiz. Wochsch. fuer Chem. und Pharm.*, an article by Fleissig appears, in which it is stated that out of eight samples of peroxide of hydrogen purchased from various German and Swiss manufacturers, only two showed an acidity below that allowed by the Swiss Pharmacopœia, which allows the same acidity as the U.S.P.; the other six having an acidity about three and four times higher than permitted. The author believes that the official amount of acid (0.036 per cent.) is entirely too small, and that an addition of 1 to 3 per cent. of acid should be allowed. This percentage, however, we consider entirely too high, inasmuch as peroxide of hydrogen is frequently used for sterilizing surgical instruments and such a high acidity might corrode these.

Fleissig further gives an interesting account about the stability of the above peroxide of hydrogen solutions. He found that after two months' standing the strength of two was reduced to two-thirds of their original peroxide strength, of four to about one-half, and of two to less than one-quarter when kept in flint glass bottles. When kept in amber bottles, he found that after standing for eight months the strength of three was reduced to two-thirds, of one to about one-third of its original peroxide strength, while four hardly



showed the presence of peroxide of hydrogen. Unfortunately the author only gives a few results about the same preparation when kept in flint glass bottles for a longer period, but from what can be learned from his data the deterioration of the peroxide of hydrogen solution is usually much greater when kept in flint glass bottles than when kept in amber colored containers. It may be stated at the same time that those preparations, in which the percentage of absolute peroxide of hydrogen was reduced to two-thirds of their original peroxide strength only, possessed a rather high acidity. This indicates that higher acidity tends to preserve the peroxide strength of peroxide of hydrogen solutions.

Since writing the above, a paper by Prof. Coblenz on this subject has been presented to the Revision Committee in which he shows that acetanilide is not necessary for preserving peroxide solutions, but also holds out against increasing the acidity because of its interfering with the usefulness of the solution in surgical work, and because manufacturers should use less alkaline glass. We agree with him on the acetanilide proposition, but we think he is wrong on the other two, for even if the amount of acid allowed by the present U.S.P. is doubled as we suggest, it will not affect the most sensitive mucous surface in the human body. And as to glassware, we have seen that both flint and amber glass possess ample alkalinity to soon neutralize the small amount of free acid allowed by the 8th Revision requirements, and when one considers the increased contact with the glass affected by the shaking during transportation, and this must be considered by the Revision Committee, the neutralization of the free acid is greatly augmented as compared with the condition presented by mere standing contact in a laboratory.

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## PRACTICAL APPLICATION OF THE TWITCHELL PROCESS OF FAT DECOMPOSITION AND RECOVERY OF GLYCERIN.

BY W. J. WARNER.

The intention of this article is to state the advantages of the process as applied to refining of glycerin and its advantages and applicability to soap making, as well as a description of the process as "worked" on a commercial basis in a plant handling 50,000 lbs. of fat per day.

The Twitchell process has superseded all others in the candle

trade, and is being more extensively used by the soap manufacturers who have recognized the advantages of the process for the recovery of glycerin, in that 95 per cent. of all the glycerin in the fat can be obtained as C.P. This will give yields from: good tallow, 9 to 10 per cent. absolute glycerin; cocoanut oil, 12 to 13 per cent. absolute glycerin; cotton oil, 10 per cent. absolute glycerin approx.; grease and poor tallow, 6 to 8 per cent. absolute glycerin.

The sweet water to be evaporated contains 15 per cent. glycerin instead of from 2 to 4 per cent. as in spent lye, and therefore about 25 per cent. as much water has to be evaporated to make crude glycerin as with soap lye. As an illustration:

The glycerin refiner is supposed to obtain 9 per cent. of absolute glycerin by weight; of the total amount of tallow saponified, actually about  $7\frac{1}{2}$  per cent. is obtained; as the tallow contained approximately 10 per cent. of glycerin the loss is considerable. Instead of having to handle 200,000 lbs. of spent lye containing 3.75 to 4.25 per cent. of glycerin, by the Twitchell process of first deglycerizing the fats there would be approximately 60,000 lbs. of sweet water containing 15 per cent. of glycerin. Besides having to handle such a large quantity, the spent lye contains salt, alkali, and fats, which are troublesome to remove; the Twitchell sweet water only has to be neutralized with lime before concentrating, consequently there is a reduction in loss of glycerin to almost nothing and a product of crude glycerin containing 90 per cent. of absolute glycerin against 80 from soap lye, which means a less expense in the refinery. The Twitchell crude is of better quality, containing but a few tenths of one per cent. of ash and C.P. can be made in one distillation, while it often requires three distillations from soap lye crude, so that a still will handle about 30 per cent. more per hour of the Twitchell crude and produce less glycerin foots.

The fatty acid obtained can be saponified with soda ash instead of caustic, which means a net saving of 12 cents per hundred pounds of fat saponified, and finally the fatty acid is of much better odor than the original stock.

In some cases it is of more importance to obtain good color fatty acid than high yield of glycerin, and for working convenience the stock is divided into three classes:

First. No. 1 tallow, mutton tallow, yellow or white cotton oil, cocoanut and palm kernel oil, white grease, olive oil, corn oil, lard, and good stearin. The color and odor are of prime importance.

Second. No. 1 and No. 2 tallow and "off" cotton oil, all the

glycerin possible is obtained consistent with good color. Neither the first nor second class of goods goes to the distillation plant.

Third. Very "off" cotton oil, house grease, olive oil foots, and cotton-seed foots go to the distillation plant and are "robbed" of all the glycerin, as color, in the Twitchell plant, is of no importance—the distilled product will be white any way.

Outside of the distillation plant the work is carried on exclusively in wooden vats or tanks, each tank numbered for convenience and record, and are designated as decomposing, acid boil, Twitchell, and storage. The decomposing and acid boil tanks are preferably lead lined. The Twitchell tanks are closely covered with snug fitting lids with an "up take" for steam. Experience has taught that certain precautions must be taken to carry out the process successfully and economically and these will be referred to at the proper time.

Assuming that a plant has just been installed, it is of prime importance to understand that in a glycerin refinery and a Twitchell distillation plant twenty-four hours make one day and seven days make a week and there are fifty-two weeks in one year, and there are no Sundays, holidays, or even lunch hours, one shift of employees relieving the other without any interruption of work. The plant is ready, a tank car of cotton-seed foots has been set about 5.30 P.M., each tank car is fitted with a closed steam coil with outside connections, the coil is connected with a steam supply in the "pump house" before which the tank has been placed, and steam turned on to heat and soften the "foots" for pumping in the morning. One of the precautions for successfully working the process is that the fat must be freed from all dirt, lime, bone, tissue, and other impurities, which sounds complicated but is very simply done. The dirt settles and is run off to the sewer. The contents of the car being softened the pump is started. A "pet cock" on the pressure side of the cylinder enables the operator to obtain a "running sample" of the contents of the car. This amounts to about three gallons. This sample is taken to the laboratory, thoroughly mixed and divided into four parts, three parts sealed in pint jars until the car of stock is run through and the fourth part for "immediate analysis" of total fatty acid. Five to 10 grammes are weighed into a 500 c.c. Erlenmeyer and 50 c.c. of a 5 per cent. alcoholic soda solution added. Boil to dryness. Add an excess of dilute sulphuric acid and boil until all soap is decomposed. Transfer to a separatory funnel using some petroleum ether to rinse Erlenmeyer. Draw water and acid off the Erlenmeyer. Pour the solution

of fatty acids in petroleum ether onto a filter and filter into a tared dish, add more ether to the water, thoroughly washing Erlenmeyer and separatory funnel, each time pouring the ethereal washings onto filter. Finally wash filter and funnel stem. You now have the total fatty acids in a petroleum ether solution in a tared dish. Dry until the loss is not more than 0.02 grammes in 20 min. at 100° C. Before the pump was started six to nine inches of water was turned into the decomposing tank and the steam turned on, an open coil being fitted in the tank. (The water is only used in starting a new plant, thereafter the decomposing tank will contain an indefinite amount of waste acid from the rest of the plant.)

Cotton-seed foots are 50 per cent. saponified when received and are "decomposed" into "black oil" by boiling with sulphuric acid. When there is waste acid in the decomposing tanks it is started boiling the same time the car is being emptied so that the saponification is broken up almost as fast as it can be pumped. After boiling an hour it is tested by allowing same to run off a paddle and should show no trace of soap. It is allowed to settle, the water and dirt going to the sewer. (If the first boil has been on waste acid the acid is exhausted when it tastes salty.) After running the settlings into the sewer add about three inches of water and 1 per cent. of sulphuric acid and boil until fat is brilliant and clear. Allow to settle. This is waste acid, tastes sour, and does for the first boil on the next car. After settling "skim" the oil from the top with a gravity suction pipe into "black oil storage tank." From storage the clear black oil is run into "acid boil tank" and shows a varying analysis: dry black oil; 50 to 75 per cent. fatty acid; 2 to 4 per cent. unsaponified; 4 to 2 per cent. glycerin; 1 to 2 per cent. moisture;  $\frac{1}{2}$  to  $1\frac{1}{2}$  per cent. dirt.

In the acid boil tank 1 per cent. of sulphuric acid and just enough water to cover the coil are added. The precaution here is that the waste acid should be 18° B, for cotton-seed foots, to obtain a good product; this waste acid goes to the decomposing tanks. The fat is boiled in the acid boil tank for about two hours, a sample taken for analysis and the stock is ready for the Twitchell tank.

It requires a man of intelligence somewhat above the average unskilled employee to be "Twitchellman." He does the "rough analysis" of the tanks during operation and keeps the records of each tank. Where there are so many tanks it is practically impossible to weigh each charge, so that the tanks are measured and weight of contents per inch calculated. Six inches of water are



run in the Twitchell tank and thirty-two inch (30,000 lbs.) black oil, cotton-seed foots being handled, 3 per cent. of the weight of the charge of black oil of Twitchell reagent is added, steam turned into the perforated coil, the trap door closed, and the Twitchellman starts his record of that particular tank. First he would ascertain the per cent. of fatty acid in the black oil as follows:

The oil would be put in an Erlenmeyer and heated until absolutely dry. Bluish vapors on the surface of the oil indicate a dry condition. Fifty c.c. alcohol are put into another Erlenmeyer and warmed, 4.1 c.c. of the dry oil are run into the 50 c.c. alcohol, alkaline blue used as an indicator, and half normal NaOH run in until neutralized. The number of c.c. of NaOH multiplied by 4 gives the per cent. of fatty acid. The result is noted in the record. This record must show the number of the tank, amount of charge and class of goods, the per cent. of fatty acid the goods contained, amount of Twitchell reagent added, the hour it started boiling, the hour it stopped boiling, the number of hours of the first boil, amount of sweet water run off, and the B° strength and per cent. of fatty acid at end of first boil, the hour of starting and ending second boil, number of hours boiling, amount of Twitchell fat run off, and per cent. of fatty acid at the finish. The length of time for the first boil is about thirty hours and should show from 87 to 90 per cent. fatty acid. After settling the glycerin water is run off into a storage tank, the number of inches and B° taken. The second boil lasts about twenty-four hours; no reagent is added to the second boil. A sample is taken and should show 93 to 95 per cent. of fatty acid, it is allowed to settle and is ready for the distillation plant. The Twitchell fatty acid, as the product is now known, shows on analysis: 92 to 95 per cent. free fatty acid; 4 to 1 per cent. unsaponifiable; 2 to 3 neutral fat; 1 to  $\frac{1}{2}$  per cent. dirt.

When the fat has thoroughly settled it is run into an intermediate storage stand and then into the "dry boxes." These dry boxes are of cast iron, built up of sections 2 ft. 6 in. square with machined edges to make a tight joint, the boxes are 5 ft. wide, 5 ft. deep, and 10 ft. long, and when the fat is dry and at about 275° F. measure 285 lbs. per inch. Each box is fitted with a closed brass coil and connections to the still. It is essential that the fat be absolutely dry when fed into the still. The distillation is carried on by live fire, each still being fitted with a perforated cross on the bottom of the inside of the still through which superheated steam is injected. A slow fire is started under the still and the vacuum pump started.

When a vacuum of 28 in. is obtained, 32 in. of fat, about 9100 lbs. are drawn into the still and the temperature gradually raised to 475° F. on the still and 575° F. on the superheater. The superheated steam is then turned into the still through the perforated cross and collection of distilled fatty acid begins. This is continued, slowly feeding fat into the still until 155 in. has been fed out of the dry boxes, approximately 34,000 lbs. The stillman keeps close watch of measurement of the distilled product because he only obtains 82 per cent. of what he feeds in, the residue gradually becoming bulky. When the "charge" has been fed in, the temperature has been raised gradually to 525° F. on the still and 650° F. on the superheater and the time has been about three days of twenty-four hours. The distillation is continued until fat begins to color, when the fires are drawn, superheater shut off, and temperature on the still allowed to drop below 500° F. Then the tar is pumped into a tar still. This tar seems to have a "flashing point" of 500° F. in contact with cold air. The safe point to pump is 475° F.; it has been pumped at 495° F. but *only* once, and when the wreck was cleaned up the yield of tar was not quite as large as it should have been. The tar still is the same as the fat still, except it is not operated under a vacuum. The remaining grease is blown out of the tar with superheated steam, the tar allowed to cool, run off and barrelled. In the meantime, the fatty acid still is again started. The process described applies only to the lower grade of fat or Class No. 3. Classes No. 1 and No. 2 do not go to the distillation plant. The Twitchell tank for handling these goods is the same as for Class No. 3 with the addition of being fitted with a steam jet immediately under the cover and above the surface of the fat. The method followed for, say, prime tallow applies to all other fats in Classes No. 1 and No. 2.

The tallow is "steamed out" of barrels into the acid boil tank and 5 lbs. of sulphuric acid to each barrel of tallow added and boiled for two hours, then allowed to settle overnight. Run water off and drop to Twitchell tank. Assuming the Twitchell tank is clean, add about  $\frac{1}{3}$  as much water as there is tallow and  $\frac{1}{4}$  of 1 per cent. of the weight of tallow of reagent and boil with open coil until test shows 90 per cent. free fatty acid, shut off open coil and turn steam through jet and keep it going all during the settling process. Air coming in contact with the fat at this stage would discolor it. When the sweet water has settled, run off, put in more fresh water and give second boil until test shows 96 per cent. free

fatty acid, shut off steam, turn on jet, and add barium carbonate mixed with a little water in proportion of  $\frac{1}{4}$  lb. barium to every 500 lbs. stock. In a few moments take a sample from cock in side of tank and test if water is neutral to methyl orange. If it is, steam may be turned off jet and water allowed to settle. The fatty acids are now perfectly stable and may be stored in wood until wanted.

The glycerin waters are treated with milk of lime until distinctly alkaline, the liquor being kept agitated to prevent settling of the calcium sulphate. The treated glycerin water, or sweet water as it is designated, is pumped through a filter press into a storage tank from which it is drawn for evaporating into crude. This can be done in an open tank with closed steam coil or in a vacuum apparatus either single, double or triple effect, to  $34^{\circ}$  B, which for Twitchell crude is 90 per cent. absolute glycerin and 80 per cent. absolute glycerin for soap lye crude. All crudes are analyzed before refining, the acetin method being generally used by the large refiners, experience showing the results obtained are more nearly accurate than by the bichromate method.

To conduct this test take:  $1\frac{1}{2}$  Gm. crude glycerin; 10 Gm. anhydrous soda acetate; 8 c.c. acetic anhydride. Boil under reflex condenser for  $1\frac{1}{2}$  hours, cool a little and dissolve tri-acetin formed in 50 c.c. warm water. Do this while still under reflex, cool and filter, washing filter well, add phenolphthalein to filtrate and neutralize excess of acetic acid with 2 per cent. solution NaOH, taking *great care* not to run over end point or let solution become alkaline locally while adding the NaOH. Then add an excess of 10 per cent. solution NaOH and boil 20 minutes. Titrate excess, also run blank on the 10 per cent. NaOH. Titration of blank minus titration of excess divided by weight of sample, multiplied by 1.533, equals per cent of glycerin.

The following yield and capacity tests (the cost test for obvious reasons being omitted) will indicate how thoroughly a plant and laboratory can check results.

Cotton foots. .703,580 lbs.	Laboratory test, 58.32 per cent. fatty acid
Reagent . . . . . 17,812 lbs.	Laboratory test, 75 per cent. fatty acid

This shows for the foots. . . . 410,333 lbs. fatty acid  
and for the reagent. . . . 13,359 lbs. fatty acid

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A total of. . . . . 423,692 lbs. fatty acid to be accounted for.

The product, based on a total distillation:

Distilled fatty acid.....	355,725 lbs.	83.97 per cent.
Tar residue .....	65,419 lbs.	15.44 per cent.
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Total recovered product.....	421,144 lbs.	
Showing a loss of.....	2,548 lbs.	.59 per cent.
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	423,692 lbs.	100.00 per cent.

The yield based on analysis of black oil:

Distilled fatty acid.....	342,595 lbs.	82.31 per cent.
Glycerin .....	5,775 lbs.	1.40 per cent.
Tar .....	65,419 lbs.	15.72 per cent.
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	413,699 lbs.	
Laboratory test .....	58.32 per cent.	410,333 lbs.
Glycerin .....	.82 per cent.	5,775 lbs.
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		416,108 lbs.

Equals a loss of 2409 lbs., or .60 per cent.

The yield based on total product handled:

Distilled fatty acid.....	355,725 lbs.	49.31 per cent.
Glycerin .....	5,775 lbs.	.82 per cent.
Tar .....	65,419 lbs.	9.70 per cent.
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Total recovered .....	59.20 per cent. of foots	
Laboratory test .....	59.55 per cent.	
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Loss .....	.35 per cent.	

The manufacturers of lard compounds refine their own cotton oil and sometimes decompose the resulting foots into black oil for economy in storage. This black oil is marketed for Twitchell, a test of a car showed: black oil, 45,460 lbs.; reagent, 2025 lbs.

Product:

Distilled fatty acid.....	30,618 lbs.	67.35 per cent.
Glycerin .....	3,173 lbs.	6.98 per cent.
Tar .....	11,028 lbs.	24.25 per cent.
Loss .....	641 lbs.	1.42 per cent.
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	45,460 lbs.	100.00 per cent.



The yield of tar on this test was excessive and indicated that some one was not familiar with the process of decomposing foots to the advantage of the distillation plant. If the process is properly handled, the quality of the stock considered, the yield of tar rarely exceeds 12 per cent. of the amount of Twitchell grease handled.

Test on house grease:

Amount of grease 30,750 lbs., less moisture 6 per cent. .... 30,566 lbs.  
Reagent ..... 675 lbs.

ANALYSIS OF GREASE.

Titre ..... 39.8 per cent.  
Saponified value ..... O.K.  
Fatty acid ..... 26.8 per cent.  
Moisture ..... .6 per cent.  
Unsaponifiable ..... .96 per cent.

ANALYSIS TWITCHELL FAT

Fatty acid ..... 92.39 per cent.  
Unsaponifiable ..... 1.96 per cent.  
Moisture ..... Trace

ANALYSIS OIL BLOWN OUT OF TAR.

Fatty acid ..... 3.86 per cent.  
Unsaponifiable ..... 96.14 per cent.

ANALYSIS DISTILLED FAT.

Titre ..... 40.5 per cent.  
Moisture ..... .8 per cent.  
Unsaponifiable ..... .65 per cent.  
Saponifiable ..... 98.55 per cent.

Yield:

Distilled fat ..... 24,182 lbs. 77.40 per cent.  
Glycerin ..... 1,360 lbs. 4.40 per cent.  
Tar ..... 2,200 lbs. 7 per cent.  
Unsaponifiable ..... 1,172 lbs. 3.80 per cent.  
Loss ..... 2,327 lbs. 7.40 per cent.

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100.00 per cent.

The loss on handling house grease was excessively high and was due to the large percentage of volatile or higher fatty acids

in the grease, which passed through the entire system of condensers, even through the duplex wet vacuum pump, appearing in billows of grease, perfectly white on the surface of the hot well. They clogged the valve chambers of the pump so that the plant had to shut down, the grease be cleaned out and new valves put in. To have collected and identified those fatty acids would have been an interesting experience, but being a commercial plant one car of such stock gave all the experience cared for.

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## SAMPLING OF GROUND SPICES.\*

BY HARRY E. SINDALL.

This subject is of considerable interest to the food chemist. It is a well-known fact that the spices as imported contain considerable foreign matter, mostly small pebbles and sand, to remove which is a difficult task for the miller, especially the pebbles. Another point to bear in mind is that some spices after being ground have a tendency to separate into layers, depending upon the difference in specific gravity of the particles. This tendency is most noticeable in black pepper.

The most satisfactory method found by the writer for the sampling of black pepper is, first, to catch about 8 to 10 oz. of the pepper as it leaves the mill at different intervals during the process of grinding. Then these several samples are thoroughly mixed together, the mixture separated into four parts by means of a spatula, one of these quarters divided into four parts in the same manner, and the division continued until a uniform sample of about 4 oz. is obtained. In proceeding with the analysis, care should be taken to mix the contents in the sample bottle before each weighing.

If ground black pepper, the hulls of which are lighter in weight than the other constituents, be allowed to remain in a pile for a few days, a sample taken from the surface would far exceed the standard allowance for crude fibre, and would run low in acid insoluble ash, while a sample taken after throwing off the top layers would run

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\* Read at the Boston meeting of the American Chemical Society, December, 1909.

just the reverse, that is, low in crude fibre and high in acid insoluble ash, due to the sand working through the product.

From experience, I have found that to get satisfactory results from ground spices packed in cartons or cans, it is necessary to procure at least four cartons or cans of the same kind, to empty the contents and to mix them thoroughly together, after which the samples are obtained by the method described above; as it is generally unfair to pass an opinion on a smaller sample, unless, of course, the product is highly adulterated, in which case the adulterant could readily be detected by aid of the microscope in any one package.

The same method of sampling gives very good results in the cases of cinnamon and ginger, although aside from the sand's working to the bottom the separation here is hardly noticeable.

With spices like mace, cloves and nutmegs, which contain considerable oil, the sampling is much easier. I have found by going over a pile of the finished products with a spatula, taking about 2 mgs. here and there, shaking up a little with a scoop, and repeating the sampling and mixing with the samples thus taken, the results obtained are good duplicates of the results obtained with samples taken by the first method, *i.e.*, when both samples have been taken from the same material.

The samples of whole spices obtained from brokers are often very misleading. They are, as a rule, very clean. On one occasion, the broker's sample ran something like 1.75 per cent. acid insoluble ash, but one bale of the material after grinding and being sampled by the first method mentioned ran between 7 and 8 per cent. acid insoluble ash. On sending my report to the broker he declared that there was some mistake and desired a sample. I sent him about fifteen pounds of the whole material out of another bale, and in due time he offered to take back the goods, which offer was immediately accepted. I should say that these bales weighed about 300 lbs. each. I merely mention this to show the necessity of taking a large sample and subdividing it.

In mustard, the best results are obtained by sampling the whole seed, for this is where the adulterant is found; especially is this the case with the brown seed. The sampling is done with an ordinary coffee sampler. About a handful of the seed is taken from each bag and examined separately under a strong magnifying glass. The adulterants here, which are readily detected, are chiefly rape, turnip,

or charlock seeds. A sample taken from any part of the dry mustard flour may be taken to test for artificial color or added starch, as these adulterants are generally worked up pretty well in the material.

Red pepper seems to be the most difficult spice to obtain a uniform sample, owing to the manner in which the pods are ground. The first method is impracticable with this spice, while the results obtained by sampling, using the second method, are about fair. The most satisfactory method to employ is the following:

A metal tube about one inch in diameter and about three feet long, with a sharp end, and so constructed that it can be forced from the top of the barrel containing the red pepper through to the bottom of the barrel, is used. The tube is emptied, inserted several times through the pepper in the barrel, the samples are mixed and subdivided until a sufficient sample is obtained for the analysis. I may say that this method of sampling gives good results with the majority of the spices where samples have to be taken from barrels.

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## CONCERNING THE AMERICAN MATERIA MEDICA.\*

BY JOHN URI LLOYD, Cincinnati, Ohio.

(Concluded from page 11.)

THE LOBELIA EPOCH.—One of the main tenets of the Thomsonians was the employment of no poisonous remedies. They aimed to exclude all mineral substances, as well as every vegetable substance that could produce death or that could be reckoned among those antagonistic to life processes. Thus the list of remedies used by Thomson omitted even such drugs as sanguinaria, or veratrum, or gelsemium.

Comes now the irony of fate! The sheet anchor of the Thomsonians was lobelia. A *lobelia course* was preliminary, in most instances, to any other form of treatment whatsoever. A vital blow was now struck by the antagonists of Thomson. *Lobelia was by them thrown into the list of poisons!* Many were the deaths reported as resulting from the heroic medication of the Thomsonians in which lobelia was shown (or asserted) to have been the chief offender. Came at last the arrest, prosecution (or as some prefer

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\* Address delivered before the Philadelphia College of Pharmacy, November 4, 1909, being the third of a series of special lectures for 1909-10.



*persecution*), and trial of Thomson, and next the famous trial of Dr. Frost. This persecution, as the Thomsonians accepted it to be, did not dismay Thomson's votaries or discourage their leader. On the contrary, it led to the more pronounced arraying of the forces of Thomson against the legalized medical profession. Thomson became a martyr in the eyes of thousands of adherents from Massachusetts to the Carolinas. A mighty rebellion had been bred among the people, having as its centre Thomson and his system of medication, its object being the extermination of the "fashionable methods" of treating disease by what was accepted as death-dealing processes imported from Europe. It was a second American Revolution, that marshalled in its ranks, as insurgents, a far greater army than had marched under the flag of Washington, an army made up of those who fought in the other Revolution as well as their descendants. The prison cell of Thomson and the prosecution of Dr. Frost became living watchwords and mighty battle cries. Forgotten was the good of established therapy. Overlooked were the sacrifices as well as the kindnesses of physicians engaged in orthodox medication. All who practised by authority were thrown into one group, and that group received the titles already mentioned, "bleeders," "blisterers," "salivaters," and even "murderers!" Most excruciatingly did they picture the process of salivation by the mercurials, the depleting effect of cantharides blister, the exhaustion of those bled of their life blood, the terrible suffering of those to whom were applied the horrible tartar emetic plaster. In every family was an object lesson.

Through it all, such men as Barton, Dunglison, Zollickoffer, Tully, and others pursued the even tenor of their way, seemingly unaffected. But yet the influence of Thomsonianism was fast undermining orthodox heroic medication. It is questionable, as this speaker looks back at those days and events, whether any other process or mode of action could have accomplished that which followed the methods of the revolutionists, although many believe that, had plain discussions in a balanced way been employed by the members of the schools of medicine, the cruel features of such medication as then prevailed would sooner have disappeared. Be this as it may, the regular medical profession generally, conceding nothing, arrayed itself against the outsiders. It protected the theory and maintained the practice based on the application of the heroic in medication.

THE CRUELITIES OF THOMSONIANISM.—But the Thomsonian

revolutionists were at a disadvantage not alone in the direction of the unquestioned energy of lobelia. Accompanying methods that they advocated partook of much that would, to-day, be called barbarism. Their large doses of compounds containing capsicum and myrrh were excruciatingly severe. Their sweating process, repeatedly applied to the same patient, was debilitating. Their "composition draughts" were almost unbearable, as this writer knows from experience. These, combined with other features of a course of Thomsonian medication, seem to have been dreaded by many of the afflicted almost as much as were the blistering, bleeding, and salivating processes of Thomson's antagonists, although the after-consequences were surely not as necessarily lasting or as fatal. Thomson had unquestionably combined the sweating methods of the aborigines of America with the emetic processes prevalent in "fashionable" medication, complicated with which was the burning as by fire of irritating materials like capsicum and bayberry. Taken altogether, the people, in escaping from one form of torture, had become involved, although to a lesser degree, in another. A *little* devil had replaced a bigger one. Then, too, it must be remembered that in the regular profession an educated man possessed of more or less misapplied learning usually conducted the ordeal test, while in the other case whoever could read or could comprehend the processes promulgated in Thomson's patent was considered fully qualified to treat disease. The one was scientifically or professionally cruel, the other cruelly unscientific and unprofessional. Helpless were the sick in the hands of either or both.

Again a spirit of unrest came upon the people. Was it necessary that the step of the man of medicine should make the afflicted shudder? From him children ran in affright. Did the treatment of disease demand this?

WOOSTER BEACH, THE "FATHER OF ECLECTICISM."—Just at this point came Wooster Beach (1833). Unlike Thomson he was an educated man. Like Thomson he was a revolutionist. Unlike Thomson he was a believer in colleges and in education. Like Thomson he had great faith in America's materia medica. A graduate of the medical department of the University of New York, his first publication, "The American Practice of Medicine," published in three volumes in New York in 1833, was rebelliously addressed to the people and not limited to the profession of medicine. Thus, although believing in college education, he defied the legalized

practitioners, in that his publication, concerning medicine, was presented to a non-professional audience. Thus, Wooster Beach antagonized both sections we have been considering. It was at once seen that he had invaded the field of Thomson, but not in any wise as his disciple, and that he had also irrevocably violated the ethics as well as the dogmas of the dominant school. The Thomsonians turned upon Beach and his followers, abusing them even more viciously than they did their old enemies, the "bleeders." The regulars raised their battle-axes. Between the two stood Dr. Wooster Beach, the prey of both. We have seen Thomson to be a man of indomitable will, determined and fearless and most fertile in resources, though illiterate. Let us now consider his rival.

Dr. Wooster Beach was conversant with the literature of the past. Barton's "Collections," Rafinesque's "*Materia Medica Americana*," Schoepf's "*Materia Medica*," the writings of Dunglison, Tully, and Zollickoffer, the Pharmacopœias of the United States of 1820 and 1830, the Proceedings of the different medical societies, these and such as these were to him familiar. With the ideal of reform but with high regard for others' efforts, he unhesitatingly selected from all these sources that which he considered best, his object being the kindly treatment of disease and a replacing of powerful remedies by those less energetic, whenever such were capable of serving equally as well. He believed in a reduction of energetic doses to such an extent that poisonous drugs, if used, should produce no toxic or harmful effect, and in the modifying of compounds in which poisons took a part, so that if the disease was not cured no dominating constituents should thereby cause fatal results.

The motto adopted by Beach and his followers, "*Vires Vitales Sustinete*" (Sustain the Vital Forces), made it necessary that these objects should be accomplished. It was the opposite of that of both his antagonists, for both depleted. Thus Beach, the antithesis of Thomson, and yet his colaborer, became the founder of an American system in medicine, antagonistic to that of Thomson. His followers believed in education, they believed in colleges, they believed in surgery and the sciences, and in rationally employing whatever could be properly utilized, from whatever source it came, whilst the methods of Thomson were those of teaching the people *directly*, through travelling agents and by person. Antagonistic were these two, in all points touching systematic medical education. The name "*eclectic*" was applied to the followers of Beach, who

claimed the privilege of selecting from any source whatever, as they saw proper, whatever could be properly utilized. They made their code of ethics the "Golden Rule" only. They did not recognize the authority of the regular profession as concerns doses or medicines. Thus, they too were "irregulars" in the eyes of the legalized part of the medical profession and needs be suppressed.

But yet the widely divergent Thomsonians or botanics (for Thomson eschewed minerals altogether) were, strangely enough, confounded by most legalized practitioners with the eclectics, whose precepts were merely those of greater kindness to the sick and a closer study of the American *materia medica* than was practised by either the Thomsonians or the regulars. The eclectics, as was their duty, even more forcibly and systematically than did the Thomsonians, fought bitterly the bleeding, blistering, mercurial purging and salivating methods still prevalent in the mother school, but not less earnestly did they oppose the sweating, the vomiting, and the heroic, enervating "courses" of the Thomsonians. But not even the eclectics of that early day could altogether escape the prevalent theories concerning disease and disease names, as well as many questionable methods, inculcated from abroad. Slow, indeed, is the process mankind travels from established error to intellectual freedom! Aiming to parallel, in a more kindly way, the processes of both the regular school and the Thomsonians, the eclectics yet believed in treating diseases by name, in the use of violent cathartics, and, as is known, in this direction they (King) introduced the "resin of podophyllum" (1835), subsequently known as the "eclectic calomel." They also believed in counter-irritants, producing thus running sores, for the purpose of relieving underlying affections, and in this direction devised their "compound tar plaster," to be used instead of old school applications of croton oil, cantharides, and tartar emetic. Whoever has seen its effect will not question its severity. They believed somewhat in *emesis*, and for this purpose devised "compound tincture of sanguinaria," and "compound lobelia powder," utilizing in the first a drug introduced by Barton, and in the other the banner drug of Thomsonianism. In view of such facts as these, as perhaps seems reasonable, the adherents of the eclectic school, coming in the height of the warfare between Thomson and his antagonists and at the most vicious period of that conflict, were viewed as *renegades* by the old-school physicians, and by the Thomsonians as *pirates*. Between 1840 and 1860 this trian-



gular war waxed hotter and hotter, each faction fighting bitterly the others, but each engaged earnestly, as they saw life's duties in their task of relieving mankind of ills, even though the attainment of the object necessitated, where heroic medication was involved, the death of the individual.

WARRING OF THE HEROICS.—But in all this, let us not forget the people who were so vitally concerned in this war of the professions. The good in each benefited the people, the wrong of one or of all injured them. Each home in America became involved, one way or the other. Under the influence of Thomson and of Beach home-made remedies increased, whilst under their combined but yet disconnected attacks criticisms of the profession became more pronounced. The cruelties of the transplanted mediæval ages, as exemplified for centuries in bleeding, blistering, and salivating, were illustrated in print and depicted in lecture, in the home, the school house, the church. The dominant school as well as the Thomsonians felt the touch. They indignantly resisted, but yet under the influence of transpiring events they lessened their doses and gradually abandoned their depleting processes. Then, at last, it was discovered that barbarism, in these lines at least, was unnecessary. But yet, all seemed to believe in fighting disease, not in preventing its occurrence.

Came, now, in the seeming day of victory, tribulation to the Thomsonians. The people had become better educated, better fed, and better clothed. The methods of times gone by would no longer be tolerated. The eclectics, too, felt the influence of the times, and discovered that their enormous and too often nauseating doses of syrups, of vinegars, and of compound tinctures were neither desirable nor necessary. They, too, began to look upon what had previously been their ideal of greater *kindness* as a process of less *cruelty*. About 1860, came the ending of the more heroic phases and processes of eclectic medication. The old school, as shown by the records, had during this period assimilated many remedies native to America, the Thomsonians had about abandoned their lobelia courses and had lessened the enormous doses hitherto employed, whilst the eclectics had discovered that disease expressions could be controlled by more kindly methods and by smaller doses than had been advocated by Beach. A great number of the remedial agents suggested by Barton, but neglected during this period by his old-school disciples, had in small doses become favorites in the eclectic school, some of them being reintroduced from

eclecticism to the school of Barton. Some remedies developed by the rivals of the school with which Barton affiliated had also become established, in many cases, the world over. To such an extent was this true as to have given (about 1860) to the major number of American remedies of the eclectics the name, "eclectic medicines."

ADVENT OF HOMŒOPATHY.—Let us now consider a phase of the American materia medica as yet neglected but of more than a little consequence. This was the advent of homœopathy about the beginning of the last century. The homœopathists believed in kindness to the sick and practised it. They believed in sanitary methods and in good nursing, and, as far as possible, these precepts were enforced. They believed in cleanliness and made this one of the tenets of their practice. They believed in small doses, even unto what, in the opinion of the other schools, was mathematical extermination of a remedy. These together constitute some phases of preventive medication. Such as this appealed to many of the more cultured portions of the people, who, in the face of ridicule, gave the homœopathic physician a hearing. About the middle of the last century the influence exerted by the homœopathist was certainly greater than was appreciated by those involved in other directions in medicine. Indeed, it is questionable whether homœopathy has been, even to the present day, credited with its due part as concerns the extermination of the conspicuous barbarisms connected with the overdosing and underfeeding of those days, and its attendant evils. Be this as it may, the advent of homœopathy at the beginning of the last century was considered so unimportant and their beliefs so chimerical as to have attracted little attention other than passing ridicule from any of the active forces we have mentioned. The chief antagonism against homœopathy came from those who had no conceptions of preventive processes but who believed that the value of medication consisted in heavy, materialistic sledge-hammer doses. By such, it was felt that homœopathy meant an abandonment of the afflicted to the enemy, disease. Those who advocated homœopathy were naturally thrown into the class of charlatans and quacks. Their opposition to heroic measures was considered as a neglect of the patient, while the theory of attenuations was incomprehensible. Nor was this view of the methods of the homœopathists restricted altogether to the dominant school, for the eclectics and the Thomsonians differed from the homœopathists as concerns dosage about as much as did the regulars. A common cause, how-

ever, threw the minority (irregular) sections together, in the face of a general enemy bound on their subjugation. Their efforts, regardless of the theories that each maintained, were, when necessary, united against professional extinction of the "irregulars." Thus the crusades went on, until about 1860 it became apparent to a few leaders in the eclectic section in medicine that not only was there no necessity for excessive doses of even innocuous drugs, but that the action of drugs, in a therapeutic sense, was far separated from active physiological shock. It became apparent, indeed, that shock to the patient, even that of post-eclectic methods, often retarded or even *prevented* a return to the normal. Thus was introduced a new epoch in the direction of American medicine as concerns the men now chiefly concerned in the evolution of the American materia medica.

### PART III.

CONDITIONS IN 1860.—Let us remember that under the aforementioned influences and the age of reason, in 1860, the physician of the allopathic or old school, who bled, blistered, and salivated, had become the exception. Indeed, the cantharides plaster and the croton-oil vesicant were at that date about all that lingeringly maintained a place in the practice of the followers of old-time heroics. Let it be remembered that the followers of Thomson had changed their name to *physiomedical*, and that they had practically abandoned the sweating and the *lobelia courses* of their founder. The eclectics, also, as the result of reflective opportunities and experimental experiences, as well as from their pharmacy studies of plant products, had abandoned many of their cruder compounds of the early days of Beach, and had become discouraged as concerns a system of therapy dependent upon the physiological action of such remedies as they had themselves introduced and developed. Even cathartics were no longer viewed with favor.

JOHN MILTON SCUDDER (ECLECTIC REVOLUTIONIST).—Came, then, John M. Scudder, a man of resources, an observer, independent, hopeful. If he did not originate the theory so actively promulgated by him, he grasped the situation, and, being at the head of the eclectic school, commanded their forces. With a courage that even his antagonists (for necessarily he had many) admired, Scudder berated the weaknesses in the eclectic school. Although he never lost an opportunity to attack wrong of outsiders as he saw the wrong, his crusade was directed more in the direction of over-

coming evils from within and correcting home faults. The "eclectic compounds" of old were within a reasonable period practically exterminated by him and his adherents. Conglomerations (syrups, compound tinctures, powders, "shotgun mixtures," etc.), with a few exceptions, were irresistibly decried. The theory of diseases being treated *by names* was combatted, both with ridicule and with argument. The *specific action* of a drug, not the guessing of the effect of a mixture, became his slogan. The individuality of a *single* remedy was studied in connection with its action in varying phases of disease expression. No longer was a disease viewed as an invading enemy known by a name, but as a rational departure from the normal, in which a systematic wrong might, under many disease names, cry for the same remedy. The doses advocated were very small, and for the therapeutic action only, never the physiological shock. Such views were, in the very nature of things, revolutionary. Antagonists from within the eclectic school called Scudder a pseudo-homœopath. They resisted and combatted him, separately and collectively. Serenely, however, Scudder, unruffled, pursued his carefully devised course. Neither vindictive nor personal was he, his object being the eradication of the questionable materia medica part of eclectic medication, and the rational application of drug remedies where it could be proven that they exerted a direct, kindly influence. Never torture a helpless man. Why should the sick be fed drugs and doses that the well cannot eat? That was his argument. He sought in homœopathic literature that which the homœopathists had in his opinion established, and he credited them therefor. He likewise sought the good that he felt had been established in Thomsonian directions, and to the followers of Thomson he gave a kind word. With no less care he searched the materia medica of the regular school, culling freely therefrom and giving credit therefor. But in it all, his doses were attenuations, as contrasted with anything preceding him in eclecticism, and many were the kindly remedies, before untouched, that he introduced to replace those more severe. He claimed that the simplest form of the remedy was the one that the physician could best comprehend, either in action or dosage, and rejected polypharmacy and its conglomerates as neither scientific nor rational. He demanded in eclecticism that the remedies employed should be simple pharmaceutical preparations, of established drugs, under their true scientific names. "Let the doctor do the prescribing and know what he prescribes," threaded his argu-



ments. In it all, however, he appealed more directly than any before him had done to the American materia medica, inaugurating a process of clinical therapeutic investigations more systematic, perhaps, than had previously been comprehended. His antagonists within the school were many, because the ideals of the past were being shattered by the man who so well appreciated both the opportunity and necessities of the present. But of this in its detail we need not speak, our object being to introduce the materia medica problem of the epoch of 1860. Through the heirlooms of the past and the processes of the then present, the eclectics had come to be the principal and the recognized developers of the American materia medica, which had once been the hope of such as Schoepf, Barton, Thacher, Thomson, and of Beach. To the plant remedies used by these men, Scudder and his adherents now added, one by one, as necessity and opportunity for investigation presented, this or that remedial agent before unknown, abandoning many in turn as being less valuable than others thus introduced. Each drug was studied after the new method, which was not that of the destruction of the drug's individuality, not that of compounding it with a number of other substances and overloading it with sugar and glycerin and other extraneous materials, but of utilizing its qualities in the most eligible and permanent form, when the plant was in its best condition. Under such methods of investigation and such ideals, the eclectic school has progressed, from the advent of Scudder, for a period of nearly half a century.

COMMERCIALISM.—It will be observed that I have aimed in this record of the American materia medica to restrict my study to influences mainly connected with what is understood as the professional side of life. Excepting the introductory complications in the direction of the pioneer in domestic medication, no reference has been made to what many consider commercialism in medicine. Alas, from beginning to end this has been too great a factor. Had this phase of my subject been incorporated into this paper, an additional chapter, fully as long as the present paper, would have been required. These so-called commercial influences were not abruptly nor yet recently thrown into the field. Upon the contrary, beginning in the earliest days of the therapy of American drugs, we find a dominating influence to be what is known as commercialism but which is very difficult to define. It was linked with the early record, in Massachusetts as well as in Pennsylvania. It was woven into some of the

efforts of conspicuous men, who wrote and copyrighted books, as well as of Samuel Thomson and some of his followers. It touched nearly every phase of professional effort throughout America, continuously pursuing its course under various phases, until about the middle of the last century, when came into play such factors as the manufacturing establishments that in pharmacy wedged themselves into the field of medicine, dominating at last, as can be perceived, many sections in manipulative pharmacy that had previously belonged exclusively to the apothecary. Of these, their influences, methods, and such, we cannot now speak. Let us not forget that in the opening of the present century and the closing of the last came another phase of commercialism in the university methods, chiefly centering in the progressive German institutions of scientific instruction. Needless is it to suggest that these influences have come to be a mighty factor at the present time and that, in the processes now in vogue, wherever patent protection is possible through the opportunities of patent laws, the contrasted attempt Samuel Thomson once made to secure protection by his patent process is insignificant. But as already intimated, these phases of the problem, entering as a thread into the very beginning and at the present time sweeping all before it as in a mighty net, can only be referred to as a subject which must not be overlooked, and cannot rest unmentioned.

WHAT OF THE PRESENT?—Thus we come to the present day. And if this history of the past be correct, we can, through this brief synopsis, form an opinion of the tortuous journey of the American materia medica from its beginning in the day of the Colonial pioneer to the present. In it, as we look back, the men constituting these antagonistic forces were incapable of comprehending the part they were taking in a far-reaching problem, whose end, in connection with the efforts of those to-day involved, is not less surely hidden from us of the present. However, into this problem, which I had hoped to make the substance of this paper, time will not permit me to enter. I must therefore close by remarking that it seems to me, when I revert to what I have said, as though the most interesting phases and side lines connected with the pharmacy (altogether neglected), the educational problems (practically untouched), the hopes, ambitions and antagonisms, the personalities of the parties involved, the many authorities, important as well as seemingly unimportant, unmentioned by me, the forgotten or overlooked ideals of

good men involved in antagonistic directions, these and such as these far overshadow that which I have presented. It has been my aim to present a comprehensive view of the important features or epochs connected with the history and the development of what is known as the American materia medica, as an introduction to that which appeals to me more deeply than does this story of the passing along.

And in this, my closing remark, permit me again to say that the features alluded to in the beginning of this paper, concerning the infinities in, and the opportunities of the American materia medica, as I view that subject and have for years longed to present it, have not as yet been reached.

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## PHILADELPHIA COLLEGE OF PHARMACY.

### MINUTES OF THE QUARTERLY MEETING.

Owing to the delay in transit facilities resulting from the severe snowstorm, the regular quarterly meeting of the College called for December 27, 1909, could not be held for lack of quorum, but five members being in attendance. Adjournment was had to January 4, 1910, when twenty members were in attendance. The President, Howard B. French, presided. The minutes of the semi-annual meeting held September 27, 1909, were read and approved.<sup>1</sup> The minutes of the Board of Trustees for September, October, November, and December were read by the Registrar, J. S. Beetem, and approved.

Mr. George M. Beringer, for the Committee on Centenary Celebration in 1921, presented the following as a tentative scope and plan for consideration:

*First.*—Scope: That the celebration in 1921 be not only a Centenary Anniversary of the College, but be so broadened as to make it likewise a celebration of the initiatory movement for establishing pharmaceutical education in America, and its subsequent development.

*Second.*—Plan: That in connection with the anniversary celebration there be arranged an exhibition in the College that shall present the work of this institution, its collection of historical matters and souvenirs, and its

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<sup>1</sup> The minutes of the special meeting held December 10 (memorial to Mahlon N. Kline, First Vice-President), were approved.

various collections of botanical and materia medica specimens and apparatus. This feature, it may later be deemed advisable to broaden out into a more extensive exhibit including manufactured pharmaceutical products.

*Third.*—That there be prepared and published in connection with this Centenary Celebration a historical work covering the progress of pharmacy in America, the history of the Philadelphia College of Pharmacy and of its graduates.

*Fourth.*—That a standing committee of the College be appointed at once to continue this work, and that in ample time before the Centenary Celebration this committee be enlarged and that it co-operate with similar committees from the alumni association and other organizations if found desirable.

*Fifth.*—Financial: (This section is reported as amended.) It is apparent that to carry out these plans there will be entailed a heavy expenditure, and in order to provide the necessary funds it is recommended that this committee be empowered to establish an account and solicit subscriptions to pay the expenses of this jubilee meeting and the College contribute thereto the sum of three hundred dollars per annum commencing with the year 1910. It is hereby provided that all moneys contributed and the yearly contribution of the College under this plan shall be paid to the Treasurer of the College and by him kept as a separate account to be known as the Centennial Fund subject to the requisition and use of the special committee to be appointed.

*Sixth.*—That the alumni be requested to set aside in each monthly issue of the Alumni Report a sufficient number of pages to be used in the continuous presentation of the centenary and the historical work of the committee to the graduates of the College.

*Seventh.*—The details and the perfecting of the plans and arrangements for the celebration, will, of course, develop as the work of the standing committee progresses, and the above is simply submitted as a tentative outline covering the broader principles that should be considered. Signed by the Committee.

(Committee) Joseph P. Remington, Henry Kraemer, Samuel P. Sadtler, M. I. Wilbert, George M. Beringer.

The report was discussed by Messrs. Cliffe, French, Remington, Poley, Sadtler, and Beringer, and after being amended was heartily approved and adopted.

The committee appointed at the meeting held December 10, 1909, to draft suitable resolutions on the death of First Vice-President Mahlon N. Kline, reported by its Chairman, Joseph P. Remington, as follows:

WHEREAS, Mahlon N. Kline, First Vice-President and Chairman of the Board of Trustees, passed from this life November twenty-seventh, nineteen hundred and nine in the full vigor of manhood:

His services to this College since he matriculated in 1868 have been, particularly in late years, constant and of the greatest value.



In public as in private station he was ever aggressive, conscientious, and true, actuated by the highest ideals and a sense of deep responsibility to a Higher Power.

He never swerved from the performance of his duty, and his loss, in the full tide of activity, has come upon us as a severe affliction.

The Philadelphia College of Pharmacy and the Board of Trustees are overcome with grief at the sudden loss which we have sustained, and we tender to his stricken widow and children our heartfelt sympathy.

(Signed) JOSEPH P. REMINGTON,  
CLEMENT B. LOWE,  
JOSEPH W. ENGLAND.

The report was accepted, and at the suggestion of the President was adopted by a rising vote. It was also agreed that the resolutions be engrossed and a copy sent to the family.

The Secretary was authorized to have a new supply of "Application for Membership with the Code of Ethics" printed, containing the amended requirements for membership.

The President appointed the following members as the Committee on Legislation: Joseph P. Remington, Chairman, M. I. Wilbert, William McIntyre, Warren H. Poley, Theodore Campbell, and Charles Leedom.

Announcement was made of the death of Mahlon N. Kline, J. B. Moore, and Bennett L. Smedley.

The Secretary stated that on account of the death of Mr. Kline, First Vice-President, several certificates of Honorary Membership were lacking his signature, when it was ordered that the Secretary of the College be authorized to fill in the missing signature, appending in a foot-note the reason for so doing.

A letter was read from Mrs. Anna M. Huntington, daughter of Thomas S. Wiegand, acknowledging the receipt of the memorial resolutions and expressing her appreciation of it and of the many and continuous acts of appreciation he had received from the College.

A communication was read from our fellow member Charles G. Dodson, donating to the College a prescription balance that was used in the store of Frederick Brown and which Mr. Wiegand used when as a young man he was employed there.

Our fellow member Joseph A. Heintzelman presented to the Library three volumes on chemistry and pharmacy—one of them edited by Professor Robert P. Thomas, a former professor in the College. The thanks of the College were tendered both the donors.

## ABSTRACT FROM MINUTES OF BOARD OF TRUSTEES.

September 7, 1909.—The stated meeting called for this day could not be held for lack of a quorum, and therefore it was decided to call the meeting for September 21, 1909.

September 21, 1909.—Meeting called to order, fourteen members present. The Committee on Examination reported the names of Harmon H. Sechler and Ralph Thomas Ulrich, P.D., as having satisfactorily passed all examination in the Pure Food and Drug Course, and they were therefore entitled to the Certificate of Proficiency, which upon ballot being taken, was awarded to them. Mr. Beringer reported that Mr. J. Redsecker Beetem had kindly consented to continue the *Maisch Pharmacognosy Prize*, under the same conditions as heretofore. He also stated that Mr. Joseph Jacobs, of Atlanta, Ga., proposed presenting annually a prize to be known as the *Maisch Botany Prize*, conditions for awarding same to be arranged for by the Board. These offers were accepted with thanks. Mr. Americus H. Moser, class of 1865, made application for a duplicate diploma, to replace the original, which had been damaged by fire. The request was granted, under the usual conditions. Professor Remington, who had recently returned from the Pacific Coast, reported that the graduates of the Philadelphia College of Pharmacy on the Pacific Coast had formed a branch alumni association, and had arranged to raise \$2000 to establish a Pacific Coast Scholarship; and Mr. England supplemented this information by stating that he had already received a subscription towards the fund.

October 5, 1909.—Meeting called to order, with fifteen members present. The Committee on Instruction reported that a special course of fourteen lectures had been arranged for, and requested the members of the Board to give their earnest support to same. A variety of subjects were to be lectured upon, and the speakers would be leaders in their respective branches. The Committee on Scholarships reported the names of nine students who had been awarded scholarships, and, upon vote, their action was confirmed by the Board. The Committee on Examination reported that Jay Dana Beck, John Joseph Bridgeman, Jr., Walter Henry Bronner, Philip Christ Dosch, Charles Duvoisin, Marie Duvoisin, Frank Gannon Ebner, Homer Willis Eakle, Henry Stites Godshall, John Elias Faison Hicks, Vastine Atkinson Keister, John Moser, Jr., Aase

Teisen (Miss.), Frank P. Van Inwegen, Howard Eakle Young had successfully passed their final examinations in the Optional Course in Bacteriology, and were entitled to special certificates of proficiency in said branch. Upon ballot being taken, they were declared eligible to have the certificate awarded them. A communication was received from the Board of Education recommending Robert Gracey, a graduate of the Central Manual Training School, class of 1909, as worthy of a full course scholarship, which on motion was awarded. Mr. Cliffe, on behalf of the class of 1884, presented to the College a barometer, that they had installed in the Chemical Laboratory, for which the thanks of the Board was extended. John Moser, Jr., was elected to associate membership.

November 3, 1909.—The Committee on Scholarships reported that after a competitive examination, Albert Worthington Moore, of Trenton, N. J., and James Vansant Hewitt, of Vineland, N. J., had passed the best examination for admission to the Dobbins Scholarship. The committee, therefore, recommended the awarding of scholarships to both of these men, as the Treasurer reported sufficient funds available to the credit of the scholarship to admit of doing so. Their recommendation was accepted. Professor Remington reported that the Wiegand Scholarship Fund of \$3000 was completed by a subscription just received from Samuel Fairchild, of New York. The Secretary was instructed to express to Mr. Fairchild the appreciation of the Board for his contribution. A communication from Miss Sarah L. Naly, class of 1895, requesting the Board to allow the women graduates of the College, who had been students of Dr. Susan Hayhurst, to place in the Museum her portrait, as she was the first woman graduate of the College, was read and the request was granted.

December 7, 1909.—Meeting called to order, with seventeen members present. Upon motion of Professor Remington, it was decided to have the members present sign and call for a special meeting of the College to be held on Friday, December 10, 1909, at ten A.M., to take action on the death of their late Chairman and First Vice-President of the College, Mahlon N. Kline; which motion was agreed to, and on motion of Mr. Poley the Board adjourned until December 14, 1909.

December 14, 1909.—Meeting called to order and fourteen members present. The Committee on Property reported the completion of a hothouse upon the roof of the Annex Laboratory. Committee

on Library reported the presentation of a copy of the Founders' Week Memorial Volume of the scientific institutions, medical colleges and hospitals of Philadelphia, which contained a very interesting and instructive account of the Philadelphia College of Pharmacy. The Committee on Announcement reported the issue of Bulletin No. 2, Volume No. 2. The Committee on Instruction presented a new roster, to go into effect January 3, 1910. By the changes made in same, the number of hours of laboratory instruction was largely increased. A large photograph of the late Thomas S. Wiegand, Librarian of the College, was presented to the Collège by Mr. Gutekunst, and the thanks of the Board were extended to him for the gift. Frank W. Fluck was elected to active membership.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

#### JANUARY PHARMACEUTICAL MEETING.

The stated pharmaceutical meeting was held Tuesday, January 18, 1910, at 3 o'clock, with Prof. C. B. Lowe presiding.

Harry E. Sindall, chemist for the Weikel & Smith Spice Co., read a brief paper on the sampling of spices (see p. 80). The paper was discussed by the Chairman, Dr. C. A. Weidemann, Messrs. E. M. Boring, Warren H. Poley, and others. In reply to questions which arose during the discussion, Mr. Sindall stated that the improved mills for the grinding of spices, including ginger and capsicum, are constructed in such a manner as to prevent the escape of the very fine material, and thus of excessive irritation of the respiratory tract, the effects generally not being noticeable after the first day; that there is not much adulteration of spices in those States having food laws, as in Pennsylvania, but in those States having no food laws, as in Maryland, there is considerable sophistication; and that one of the most common examples of sophistication is that furnished by ground ginger, the method being to add capsicum to ginger which has been previously partly exhausted for other purposes.

John K. Thum, apothecary at the German Hospital, Philadelphia, read a paper giving abstracts of the Researches of the Pharmaceutical Institute of the University of Berlin for 1908, which will be published in a later issue of this JOURNAL. The paper elicited queries and comments from Professor Lowe, and Drs. Weidemann and Osterlund.



Prof. Henry Kraemer called attention to some of the features of the third and latest edition of the Pharmacopœia of Japan, stating that inasmuch as the revision of our own Pharmacopœia is being considered from so many points of view, a more intimate knowledge of the various foreign pharmacopœias is desirable. He stated that the Japanese Pharmacopœia is issued by an edict of the Government, that it is a very practical and well-arranged work, and is essentially a pharmacist's book.

Among the features to which he particularly referred are the following: The aromatic waters are mostly made directly from the drug by distillation; extracts, tinctures, and wines are made by maceration; sesame oil is directed in the formulæ for ammonia liniment and lime liniment; formulæ are given for the preparation of medicated cottons and gauzes (telæ); in addition to antidiphtheric serum, antitetanic serum and tuberculin are official; besides the ferments, pepsin and pancreatin, diastase is official; to the assay processes identity tests for the alkaloids are usually appended; the descriptions for vegetable drugs are very simple in some cases, as that for licorice root, but when the drug requires special consideration the description is given in more detail. Of the vegetable drugs the following were mentioned as of special interest: *scopolia* preparations replace those of *belladonna*, although *belladonna* leaves are official; under *ipêcac* directions are given for removing the wood before using the drug in the making of preparations; three starches are official, that derived from the potato tuber, one from the root of *Erythronium dens canis* L. and one from the root of *Pueraria thunbergiana* Benth. Other of the official drugs were also mentioned, as follows: the rhizome (root) of *Phytolacca acinosa* var. *esculenta*, the whole plant of *Taraxacum officinale* var. *glaucescens*, the rhizome of *Coptis anemonefolia* and of other species of *Coptis*, the rhizome and roots of *Gentiana scabra* var. *Buergeri*, the wood of *Picrasma quassioides*, the seed of *Prunus armeniaca*, and the leaves of *Prunus macrophylla*. Another noticeable feature is the number of American and European drugs which are recognized, as the tuberous root of *Aconitum Napellus*, *cascara sagrada*, and *hydrastis*. Among the official alkaloids, *agaricine* was noted.

The terms and general directions used throughout the text are explained in the preface; the metric system is used, and quantities given in the formulæ are in parts by weight. In the appendices

are given a list of the common official medicines which should always be kept in every dispensary; a list of the official medicines which belong to the class of poisonous medicines, which should be kept with special care and separated from others; a list of the official medicines that belong to the class of strong or energetic medicines, and which also should be kept with care separated from others; and a list of medicines together with their doses for an adult.

In commenting on some of the features to which Professor Kraemer called attention, Prof. I. V. S. Stanislaus said that he thought it rather remarkable that antitetanic serum and tuberculin should have been made official in the Japanese Pharmacopœia when they are used so little in practice as curative agents. With regard to the preparation of aromatic waters, he said that, generally speaking, the oil does not represent the drug or contain all of the odorous principles, as in the case of oil of rose where the benzene alcohol, one of the constituents which gives to rose its peculiar odor, does not come over with the distillate.

Mr. Thum expressed the opinion that medicated gauzes should be admitted to the U. S. Pharmacopœia, and stated that the official standards for ether are not sufficient to insure an ether of proper strength and purity for anæsthesia. He said that the best ether on the market varies, and that the next edition should recognize an ether for anæsthesia, the standards for which should be very high regardless of cost, although he thought that ether could be manufactured more cheaply now than formerly. Remarks were also made by Professor Lowe and Messrs. Boring and Poley.

FLORENCE YAPLE.

Secretary *pro tem*.

# THE AMERICAN JOURNAL OF PHARMACY

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## PHYSIOLOGICAL STANDARDIZATION: ITS VALUE AND LIMITATIONS.

BY HORATIO C. WOOD, JR.,

Associate Professor of Pharmacology, University of Pennsylvania.

You have probably heard of the old Irishman who, when asked if he could play the violin replied, "Bedad I don't know; I have never tried." Most men are not so modest in regard to their ability as pharmacologists. It is one of the peculiar traits of the human intellect that there are certain things that almost every man believes he can do as well naturally as those who have made them the pursuit of a lifetime. Among these occupations that are supposed to be Nature's free gift are preaching, boat-sailing and physiological assaying.

It is not mere jealousy, however, that excites the indignation of the professional waterman at the conceit of the amateur sailor, it is the knowledge that human lives are the price of his presumption. So I trust you will pardon me if my language should become emphatic, for you realize as do I that men are paying, if not with their lives, at least with their health, for the ignorance of self-styled pharmacologists.

I shall not attempt, therefore, to discuss with you this afternoon how to make biological assays, for those of you who are trained in the methods of pharmacology need no instruction from me, and to those of you who are not it would be impossible to impart any useful information concerning the biological assay in the short space of a single afternoon. I purpose speaking to you, not as to those who are meditating making these tests themselves but as to those who are

weighing the advisability of introducing such tests into their business and who wish to know the likelihood of the innovation's paying, and are wondering where they can find some one qualified to undertake the work. To such I shall try to give some facts that may serve as an aid in deciding whether the biological assay is of sufficient value to justify the expense involved, by an unprejudiced summary of what in my opinion may and may not be hoped from it.

And first I shall speak of its limitations. We sometimes read of the physiological test being used as a control of the chemical assay. To attempt to corroborate the findings of the chemist by a test on the living animal is about as sensible as it would be for a navigator to regulate his chronometer by an Ingersoll watch; the relative accuracy of the chemical and physiological assay is about the same as that of the \$200 chronometer and the dollar watch. The latter is in its place, however, a very useful apparatus; a cheap watch is better than none at all.

The experienced chemist can obtain accurate results because he knows the common sources of error which are likely to vitiate his conclusions and how to guard against them. In biological assay we know only of a few of the possible causes of inaccuracy and even some of these we cannot exclude.

Foremost among the difficulties that destroy the accuracy of the biological test stands that mystery of which we know nothing but to which we give the name of idiosyncrasy. Every physician recognizes well the inexplicable susceptibilities of certain persons to certain drugs, but many scientists forget that man is after all an animal and that the same biological facts hold for the humbler as for the highest type of mammal. After we learn to appreciate this possibility of mistake the only means that we have to guard against it lies in the repetition of experiment sufficiently often that by the laws of chance any exceptional result will not greatly modify the average. Think of a chemist who would make routinely nine or ten assays of the same specimen and then expect an error of 10 or 20 per cent.

Another well-known but frequently neglected fact is that disease has a potent influence on the reaction of the economy to chemical agents. Dogs and frogs are as likely to be sick as are men, indeed more so. It is often quite impossible to recognize an abnormal condition in an animal that you see but once for a few minutes immediately before the experiment; against this fallacy the only defense we have is again the multiplicity of observation.



From external conditions which affect the result it is easier to protect ourselves if we but know those which are likely to influence the effect of the drug under study. The difference in the susceptibility of frogs to many poisons in summer and winter is well known. Edmunds and Hale have conclusively shown the importance of this in the assay of digitalis, and my own experience has convinced me of the futility of hoping for accuracy in the assay of ergot on a hot summer day. There are many other circumstances whose importance may be great but of which we know but little, as age, sex, breed, nourishment, etc. The difficulties arising from imperfect absorption, from the presence of antagonistic principles in crude drugs, of the perversities of inanimate objects, and similar technical obstacles I shall not occupy your time in discussing. I wish to emphasize, however, that even with the utmost care and with frequently repeated experiments we must be prepared for an error of from 10 to 15 per cent. or even more.

Believing as I do that the biological assay is less accurate, more difficult, and often more costly, I cannot see how it can hope to compete with the chemical as a routine means of standardization. But when we recall that there are over a hundred crude vegetable drugs, including some of our most potent poisons, recognized by the Pharmacopœia, for which we have no official process of assay, it is evident that there is need for a subsidiary method of determining the comparative activity of our materia medica. It is probable that for some of these a chemical test will be provided in the next edition of that magnificent work which stands as incontrovertable evidence that in certain lines, at least, the sister professions of America are second to none in the world, but for many of these substances there is little hope that any reliable chemical test will be devised in the near future. Some of them are as unsuited for the pharmacologist as they are for the chemist, but many of them, and especially the more powerful ones, should lend themselves comparatively readily to the physiological assay. Among those which seem pre-eminently suitable for biological standardization I may mention such important remedies as digitalis, squill, apocynum, aspidium, cannabis indica, ergot, gelsemium, lobelia, and veratrum, etc. If I can show you that the pharmacologist is able to solve many of the vexatious pharmaceutical problems that cling to these drugs, will you not grant me that he is worthy your most earnest encouragement in his work?

Let us try, therefore, to peer into the future and see what prospects of success lie before him who embarks on this enterprise. We can hope to penetrate the dark mist which hides from our vision what is to come, only through the telescope of history, and as a foundation for the prophecy of the destiny of biological assay I wish briefly to review with you some of the past accomplishments of the art.

Before we seek to gauge the progress that has been made we must have a clear understanding of the goal towards which we are striving, of the questions which we may hope to answer by the method. First and foremost of course we desire a means of determining the relative potency of individual samples of drugs; in other words, to be able to distinguish between a specimen of good quality and one of poor grade. But allow me to emphasize with all the vigor that I can that this is not the ultimate nor even the chief aim of the real pharmacologist. The idea which is prevalent, that when a pharmacologist has worked out a method of assay simple enough to be commercially available and accurate enough to be scientifically useful, he has fulfilled his whole duty to the pharmacist, is an error due I believe largely to the commercial dominance in the field of investigation.

The man who is engaged in the drug business as a business is satisfied if his pharmacist enables him to sell reliable goods, that is, to manufacture preparations of uniform strength; but the scientific pharmacist wishes an answer to many and various questions that have been perplexing his profession for years. He wants the biological assayer to aid him in discovering the most favorable condition under which the plant may be grown and the best method of collecting and preserving the crude drug; the most useful solvent for extracting its activities; the rate of deterioration which takes place both in the crude drug and its galenicals, and the methods of delaying these changes. Last but by no means least the pharmacologist can be of invaluable assistance in working out methods of chemical standardization.

Keeping these objectives before us, let us briefly review what has been accomplished with some individual drugs along the lines I have mentioned.

Because of its great practical importance, and of its well-known liability to variations, and because it produces certain well-marked effects which would seem to make it an especially suitable object for physiological testing, digitalis has been more studied from the

standpoint of biological standardization than any other drug. As long ago as 1866 Fagge and Stevenson attempted to determine the relative activity of several members of the digitalis group by their toxicity to frogs. Their studies, however, were undertaken chiefly with the idea of comparing bodies closely allied physiologically to digitalis, as antiarin, helleborein, and the like, rather than preparations of digitalis itself. Apparently it was fifteen years later that the idea of using a similar method for determining the quality of preparations of digitalis was first projected. In the year 1881, two papers were published upon this subject, one by Bennefield, who used a method based upon the quantity of digitalis required to kill a rabbit, and the other by Frankel who based his calculations upon the changes caused in the movements of the dog's heart. It is not my purpose to enter into the vigorous discussion which has been waged as to the relative value of different methods of standardizing digitalis; I wish only to express my conviction that no method of biological assay, the conclusions of which are expressed in units of a standard preparation, can be held to be satisfactory. The result of the physiological test must be such that it can be expressed in absolute language, perhaps like that which is used to express the standard for diphtheria toxin: the amount required to kill a certain weight of a certain animal in a given period of time, and under conditions which are accurately described.

The first result of the physiological **assays** of digitalis was to yield scientific proof of a fact that was **already** shrewdly guessed, namely, that different samples of the drug varied enormously in their potency. It has been shown by a large number of investigators that the ordinary range of variation of different specimens of digitalis is anywhere within a limit of 400 per cent. That is, that the strongest sample will be about four times as active as the weakest. Farr and Haynes found that the prejudice in favor of the second year leaves of the *Digitalis purpurea* is only partially justified; for while it is true that in the samples they examined the leaves of the second year's growth were slightly more active than those of the first year's growth, the difference was only as 8 to 10. Focke has shown that the leaves of the wild digitalis are more potent than those of the cultivated plant, and in the samples he examined Ott found that those which came from Bohemia were more potent than those from other parts of Europe. Wolff found that the deterioration of the crude digitalis leaves was due almost solely to improper methods

of storing; if the leaves were dried in vacuo at a temperature of about 100° and afterwards hermetically sealed, they retained their activity unimpaired for a long period of time. Dixon and Haynes were unable to observe any deterioration in a tincture of digitalis which was kept for four months without special precaution. Houghton found, however, that the present official liquid preparations of digitalis lost about 10 per cent. a year, although the tincture of strophanthus seemed permanent. A higher percentage of alcohol than at present required seemed also to be shown by his work to be desirable.

Bennefield made an attempt to determine the quality of digitalis tincture by the percentage of the solid extractive matter which it contained, but found that this bore no relation to the physiological activities of the drug. In 1895 Keller described a method for the chemical assay of digitalis, based upon its percentage of digitoxin. Ziegenbein, and also Famulener and Lyons, found, however, by means of biological tests that Keller's method of assay was unreliable. In 1904, Barger and Shaw confirmed these findings, and showed that the inaccuracy of Keller's method depended upon three facts: first, that it did not extract all the digitoxin; second, that it did not isolate the digitoxin in a pure condition; third, that digitoxin is not the only active ingredient of digitalis. Which reminds me of the story of the little girl, who when asked if she was going to Maggie Jones's party said, "No, she did not like Maggie Jones, she had nothing to wear and besides she was not invited."

This hasty summary of what has been done through biological assay of digitalis seems to me to show great advancement in our knowledge of an extraordinary complex subject, for while we may be disappointed at the slowness of the progress it is undeniable that great advance has been made. Of the questions which we saw were within the province of the assayer to consider, all have been answered, if not with absolute finality, yet within the limits of scientific probability, except only the means of standardizing the drug chemically. He has told you how you may distinguish between active and feeble samples of digitalis, he has told you where grow the best quality of leaves, when to gather them and how to keep them with the minimum of deterioration, he has told you the best menstruum to extract their virtues and of the necessity of dating digitalis galenicals. I am convinced that did the pharmacist but hearken to the advice of the pharmacologist as to the manufacture



of these preparations the clinician would cease to complain as to the quality of the tincture of digitalis which is dispensed to his patients.

Another drug which has attracted attention as a worthy object of physiological assay is ergot. The earliest effort to ascertain the quality of ergot by biological means appears to have been made by Grünfeld with the method suggested by Prof. Kobert, of determining the dose necessary to interrupt the circulation in the comb and wattle of the rooster. Little practical use was made, however, of the biological method in connection with ergot until 1898, when Houghton published an account of some results of cock's comb assays practiced commercially. The workers with this drug have not been nearly so numerous as in the case of digitalis and the results are correspondingly meagre. Beyond the mere proof of the variability of galenical preparations of ergot almost nothing of value was added to our knowledge of this drug until within the last few years; from a pharmaceutical standpoint no more was known of ergot at the opening of the present century than fifty years ago.

Within the last three or four years, however, it has been the subject of more study and some very interesting facts have been brought to light by the work of Kraft, of Barger and Dale, of Edmunds, and others. In the experiments which have been going on in the pharmacological laboratory of the University of Pennsylvania during the past two years we have been able to show that the inferior quality of the fluidextract of ergot which is at present on the market is due largely to changes which take place after its manufacture; even in hermetically sealed bottles the loss of potency is at the rate of about 3 per cent. a month, and if the preparation is not guarded from contact with the air the deterioration may amount to 50 per cent. in a few weeks. Our recent evidence, although not conclusive, inclines us to the belief that, contrary to the popular opinion, the crude drug does not weaken so rapidly as the fluidextract. We have also worked out a method of chemically determining the quality of ergot which has so far yielded us figures fairly parallel to the results of physiological tests of the drug.

I should like to mention one other individual example, very briefly, of progress in a pharmaceutical subject through physiological methods; not so much because of the importance of the drug in question as for an evidence of what can be accomplished by a single

capable worker in a comparatively short space of time. I refer to the contributions which have been made by Dr. Reid Hunt to our knowledge of the thyroid gland. In two interesting communications, published within a year of each other, Dr. Hunt described a method for standardization of the thyroid gland based upon principles which were absolutely new to biological assay; showed the wide extent of variations in the commercial samples of the drug; showed that the activity of the thyroid body varied not only with the species but with the age of the animal from which the glands were obtained, and the influences which special feeding of the animal may have upon the activity of the gland; and, finally, determined that with unsophisticated glands the percentage of iodine was an accurate indicator of the quality of the drug. Truly, through this one man's efforts we have been led with dramatic suddenness from absolute darkness to the brilliancy of almost complete knowledge.

I have chosen as examples of what may be accomplished three drugs which have yielded some interesting results, but I must confess that outside of these instances which I have mentioned little of importance has been added to our knowledge of practical pharmacy through physiological investigation. When we consider how much might have been done, and how little has been done, the pharmacologist may well bow his head in shame at the neglect of so fruitful a field. We cannot plead that the idea of biological assay is so recent that there has not been time enough for its development. More than forty years have elapsed since the method was earnestly suggested and for more than twenty-five years it has been more or less systematically applied in various laboratories of the world. There certainly has been time enough in this half century of an intellectual progress, whose rapidity has never been equalled at any stage of the world's history, for the development and application of the method of biological assay to a dozen drugs instead of one or two.

But the laborers in this field have been so pitifully few that one should wonder not at the smallness of the harvest but at its abundance. We are, however, not altogether without excuse for the neglect of this field. Pharmacology is a young science—men sometimes forget that the first pharmacologist in the modern sense of the word is still living and teaching—and in the enormous mass of problems the accumulations of centuries, many of them of fundamental importance for its own development, which the world hurled

at the infant science, it is little marvel that some have been neglected. And even to-day the little handful of men who are working in this line are being assailed on every hand to answer the widest variety of questions. We are supposed to tell immediately the exact physiological effects of new synthetics which are being dumped upon the profession by the wagon-load, to discover the laws which govern the relation of chemical composition to physiological action so that the chemists may dump their synthetized garbage upon us still more rapidly, we are asked to discover at once specifics for various fatal fevers which the growing intimacy with the tropics has made so important to civilized peoples, to furnish the means to the physiologist and pathologist for solving some of the obscure problems of their branches, to explain to the clinician the mode of action of the ancient remedies, and to convince him of the worthlessness of drugs whose inertness is hidden beneath the traditions of antiquity or the glitter of the advertiser's gold, to suggest new uses for old drugs and new drugs for old diseases, to—— Can you condemn pharmacologists that they have failed to recognize the importance of biological assay to practical medicine?

As a result of this the development of the physiological assay has been left largely in the hands of the manufacturers and they have been more interested in developing it as an advertising asset than as a means of standardization. This may seem a rather sweeping accusation but I think it no great exaggeration. You would think it strange, to say the least, if a manufacturing pharmacist were to entrust all his chemical work to a young man with no more experience than is gathered in the ordinary course in a pharmaceutical college; and if this same manufacturer were then boastfully to advertise his chemical control of all his products you would hardly hesitate to criticize. Yet the situation in many of the so-called pharmacologic departments of wholesale druggists is even worse than this. You know that practical experience is necessary before a man can be trusted to turn out reliable chemical assays, no amount of book learning can take the place of the actual manipulation of the process. If this is true of chemical work in which we can put down in black and white the difficulties one is likely to encounter, how infinitely more necessary is practical experience in a field where we know almost nothing of the way in which we may go astray, where reliable methods have not even been worked out, and where we are

dealing with a living reagent of whose delicacy of response we can never be sure.

"But," say these men in defense, "it is not because we do not want them, but because we cannot get them, that we do not have competent experts in this line." To this I reply that the reason the manufacturers cannot get trained pharmacologists is because they will not pay the necessary price. I confess that at present the cost is large. The demand for pharmacologists to-day is greater than the supply and as is always the case in such conditions the price is high. Suppose a young pharmacologist holds a position at a university and is earning say \$1500 a year, with congenial surroundings and good prospects for advancement, would he not be a fool to change such a position for a commercial one with the attached obloquy which justly or unjustly is associated with such work, in which the likelihood of further advance is remote, for practically the same financial recompense he is receiving for his university work?

To tempt the scientist into commercial work requires two things: a larger salary than he is likely to receive for educational labor and a readjustment of the conditions which maintain in the laboratory of the drug manufacturers. He must cease to be regarded as a sort of attache to the advertising staff and be allowed at least a degree of scientific freedom. One of the chief reasons for the odium which pharmacologists consider inseparable from a commercial position is that the investigator must publish nothing or only that which his employer considers to be to the advantage of his business interests; in other words, his work is limited not only as to its kind but also as to the results he shall obtain. Need I tell you that such a situation is utterly abhorrent to any man of scientific instincts?

I see no reason why this last trouble should not be easily eradicated; just inject a little really ethical integrity into your business and the matter is arranged. As to the monetary question, I am not in a position to tell you whether you can stand the expense and continue to do business or not, that you must answer for yourself.

If not, the problem becomes difficult, but it must be solved. If the next edition of the United States Pharmacopœia includes more biological tests, and there is evidence of a growing sentiment in this direction, either the manufacturer will have to find some one to make these tests or else stop making preparations of these drugs; for if I read the times aright the inexperience of their experts is not going to be accepted by the Government as an excuse for the failure



of their products to come up to the standard. Either the assay must be done rightly or the manufacturer is going to have trouble with the law.

While the number of drugs which require biological assay may seem at first thought too small to justify the outlay necessary to obtain a man competent to do the work, there are so many other ways in which a pharmacologist may make himself valuable, as, for instance, the introduction of new drugs and new preparations, that there is at least a strong possibility of such an expert being a paying investment even at present prices. If the manufacturer can afford to pay these necessary salaries let him step right up and do so and the dilemma is evaporated.

If he cannot, I see but two possible alternatives: either the manufacture of preparations of digitalis and other drugs which shall be biologically assayed will have to be left in the hands of the specialists, as antitoxin is now, or else some artificial means of increasing the supply of pharmacologists will have to be adopted.

To fulfil this latter the first step is to provide some place where the willing novitiate can obtain his education. At present the training of a pharmacologist is almost universally an individual one; that is, some young seeker for knowledge enters into the laboratory of some older man who has previously trod the same path and labors and patiently accepts the simpler duties which he is fit to perform, watching his senior and gradually imbibing little by little a working knowledge of the art; much the same process of education as the old fashioned apprentice was led through in the bygone days. Whether or not our modern more systematized and more rapid method turns out any better or as good workmen is a question open to debate, but at least it turns them out more rapidly, and quickness is the great desideratum in the eyes of the young America of to-day. The change of conditions occasioned by the passage of the various food and drug acts all over the country, and the consequent compulsion to abide by the standards in fact as well as in name, has led to the formation of courses intended for the training of experts in this line similar to the one established a year or two ago at this venerable College for nearly a century the pioneer in all movements looking to the uplift of the profession of pharmacy.

But who is to give a course of training in methods of biological assay? Are the schools of medicine likely to do so? I think not, for while I grant you they are at present the best equipped institu-

tions for such work, the medical profession generally does not feel the pinch of necessity with quite the same sharpness that do the pharmacists. Will the schools of pharmacy undertake the task? Can they? I hardly think so unless some special aid is rendered them. Pharmacists generally speaking, teachers, retailers, and wholesalers, are only beginning to appreciate that under modern conditions *all* education has become a matter of philanthropy, not to say charity. The world has long believed that a young man should be offered as much as he wants of general education and culture, at his own price, as is shown by our public school system, with its normal schools and high schools, and by our numerous partially endowed colleges. But we of to-day have gone a step further than our fathers and are giving young men not only their general education but are giving them their technical training fitting them for their life-work, free of cost. You find the great universities of the land supporting their chemical departments, their engineering courses, their medical schools, etc., each being run at a large annual loss, and their continued existence made possible only through the aid of their alumni and friends. But the schools of pharmacy are attempting to struggle against this universal trend, to keep up the standard of their profession and yet make those who enter it pay for the privilege. It is a lost cause; either you must be content to see the apothecary little by little degenerate into a minor merchant, or you must come to the financial assistance of your institutions of learning. There is no more practical way to begin than for you who most poignantly feel the need of pharmacologists and who have been able to gather the means for the satisfying of your ambitions to establish in connection with your alma mater a post-graduate department for the training of young men for this work. The necessity is yours, the opportunity is yours, what will you do with it?

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## ASSAY OF MEDICINAL PLASTERS.

BY FREDERICK B. KILMER.

Comparatively little literature has appeared in scientific publications in respect to the analysis or assay of medicinal plasters made with an India rubber base.

The enactment of the Federal Food and Drugs Law and the

enactment of similar laws in the various States has brought the subject to the attention of the pharmaceutical chemist, and at the present time the subject is one of moment to both the medical and pharmaceutical professions.

Prior to the issuance of the last revision of the Pharmacopœia, no authoritative process of assay of any medicinal plaster appeared in that work. In this revision a process was given for the assay for mydriatic alkaloids in belladonna plasters made with a rubber base. Those who have given attention to the subject will no doubt agree with the statement that has been made, that it is a very difficult matter to assay some kinds of medicinal plasters made with a rubber base. It is a well-known fact that for some such plasters no method is known for the assay of the drugs contained therein, for the reason that the drug used has no alkaloid, or no alkaloid or no inorganic substance capable of definite measurement.

In other varieties of these plasters the presence in the rubber base of resinous or other matters is such as to confuse the results and make them of doubtful value. In the laboratory of the writer considerable work has been done in the assay of this class of preparations, and in our work we possess some advantages over any outside laboratory, in that as the laboratory is connected with the manufacturing department it is at once known exactly what has been put into a plaster, and it is only necessary to provide methods of assay that will give the results looked for. The methods and processes which I herewith present are simply those which have been worked out in the laboratory, more particularly as a check to manufacturing processes. They are presented for what they may be worth, with the hope that other workers may have an opportunity to try them and thus bring out information of value to those interested.

#### BELLADONNA PLASTERS.

For belladonna plasters we use the assay method of the eighth revision of the United States Pharmacopœia. This process, with some slight modifications, has been entirely satisfactory in our laboratory, where assays running perhaps into thousands have been performed. It has also had the benefit of an extended check test, in that in this laboratory it is our practice to first assay the drug used in the manufacture of the plaster and then the solid extract made from the drug; the mass itself is made up of the assayed extract taken in an amount which will give in the finished product the desired percentage

of alkaloid required in the plaster, and by this method of plaster assay the results have shown that in mixing several hundred pounds the assayed plaster corresponds with the calculated amount, often to the second and third decimal.

#### SALICYLIC ACID PLASTER.

The method which we use for the analysis of salicylic acid plaster is a colorimetric method with ferric chloride. The depth of color imparted to a ferric chloride solution by a measured amount of a solution of the plaster is compared with that of a measured quantity of a standard solution of salicylic acid of known strength. Colorimetric methods are always subject to some variation, chiefly on account of errors of eyesight; but because of the presence of resinous materials in rubber plaster masses, no other method has been found to be satisfactory and we have found that in our hands, by careful manipulation, this color comparison method has given sufficiently satisfactory results.

*Plaster Solution.*—Weigh out accurately about 5 Gm. of the plaster cut into rather small strips. Place on the table two beakers of about 150 c.c. capacity each. Designate them as No. 1 and No. 2. Place the weighed strips of plaster in No. 1. Add to it 50 c.c. of chloroform. Stir gently until all the compound is removed from the plaster-cloth and in solution. Pour the syrupy solution into beaker No. 2. Add to this in No. 2 beaker, 40 c.c. ordinary 94 per cent. alcohol, stir thoroughly to precipitate and coagulate the rubber and allow it to stand. Pour off all possible of the liquid into a glass stoppered graduate 250 c.c. flask. The rubber should be worked up into a compact mass so that no particles are carried over when the liquid is poured off and all possible liquid should be pressed out of the mass with a glass rod. To the plaster-cloth in beaker No. 1 add 25 c.c. chloroform. Stir carefully and thoroughly until all the remaining plaster-mass is dissolved from the cloth and sides of the beaker. Again pour off the solution into beaker No. 2, which contains the precipitated rubber. Work up with glass rod until all of the rubber mass is again in solution in the chloroform. Now reprecipitate the rubber from this solution with 20 c.c. alcohol, working up with rod and pouring off as before, mixing the fluid with the first portion in the flask. Once again wash the cloth in beaker No. 1 with 25 c.c. chloroform. Pour off into No. 2 beaker, dissolving again the rubber mass in it. Re-precipitate the rubber from



it with 20 c.c. alcohol as before, pour off and mix the decanted fluid with the other two portions in the flask which now contains all of the salicylic acid in solution. Fill the flask up to the 250 c.c. mark with alcohol. Remove the cloth, which should now be white and clean, from beaker No. 1, allow it to dry spontaneously, and weigh. Subtract its weight from the total weight of plaster used, thus ascertaining the weight of plaster compound taken for assay.

*Standard Salicylic Acid Solution.*—Weigh out exactly 0.5 Gm. pure salicylic acid and dissolve it in 50 per cent. alcohol. Transfer to a 500 c.c. glass stoppered graduated flask, rinse out the vessel, in which the acid was dissolved, with repeated portions of 50 per cent. alcohol, adding each portion to the solution in the flask. Make up to the 500 c.c. mark with 50 per cent. alcohol, shake thoroughly. One c.c. of this solution contains .001 Gm. salicylic acid.

*Analysis by Color Comparison.*—For this work we use two large test-tubes of similar internal diameter ( $1\frac{1}{4}$  inches by 6 inches long). Any pair of glass cylinders or tubes will suffice, but small diameter test-tubes do not give sufficient thickness of solution to secure enough depth of color with transmitted light. Place these tubes side by side. In a beaker place 100 c.c. distilled water to which add one drop ferric chloride solution U.S.P. Stir the liquid and pour into each of the test-tubes 50 c.c. of it. Designate them No. 1 and No. 2. Now add to No. 1 tube from burette, sufficient of the standard salicylic acid solution to give a strong clean wine color. Stir with a glass rod after each addition of the acid solution. Multiply number of c.c. used by .001, which will give the weight in grammes of salicylic acid used in tube No. 1—the standard. Now add to tube No. 2 from another burette sufficient of the plaster solution exactly to match the color obtained in tube No. 1. This plaster solution must be added a little at a time and the solution in the test-tube well stirred with a glass rod after each addition. When the matching point is nearly reached it may be necessary to filter off the contents of the test-tube No. 2. Clean the tube and replace the fluid, proceeding thereafter to add the plaster solution a drop at a time. The reason for doing this is that the small amount of resinous matter separated from the solution may cloud the mixture in No. 2 test-tube and interfere with the color judgment. By closing one eye and observing the colors while holding the tubes side by side between the eye and a window the colors can be matched very closely. It is obvious that the quantity of plaster solution used

contains the same amount of salicylic acid as was used in tube No. 1. That quantity is already determined by means of the standard solution. Therefore 250 (total amount of plaster solution) divided by the number of c.c. plaster solution used in tube No. 2 and the result multiplied by grammes acid found to have been used in tube No. 1 gives the weight of acid in the plaster compound. Multiply the weight of the salicylic acid found by 100 and divide the result by the weight of the plaster compound used. The result is the per cent. of salicylic acid present.

This method has been used chiefly with plasters containing 20, 25, and 30 per cent. of salicylic acid. When very small percentages are present it will, of course, necessitate the addition of a much larger quantity of plaster solution to tube No. 2 in order to secure the same color as that of No. 1 tube and consequently the color of tube No. 2 will be unduly diluted. If by trial this is found to be the case, it will be necessary to prepare a weaker standard solution or else a more concentrated plaster solution. This matter can readily be determined by trial.

In making these assays it is well to make three of each and to take the average. By doing this we have been able to get satisfactory results, the natural variations of color judgment balancing one another and the result being nearly correct in the average of the three determinations from one lot of plaster solution.

#### MERCURIAL PLASTER.

The requirement of the U.S.P. is that this plaster shall contain 30 per cent. metallic mercury.

*Method of Assay.*—Weigh out about 5 Gm. of the plaster, cut it into rather small strips. Place these in a beaker and add about 50 c.c. benzol. Stir well for some time to soften and dissolve the compound. Pour the solution off into a beaker of about 200 c.c. capacity, allowing the cloth to remain in the first beaker. To the cloth in the first beaker add repeated portions of about 50 c.c. benzol, stirring well and pouring off each time into the second beaker until the mixed solutions amount to about 200 c.c. The clean cloth is now allowed to dry in the air, weighed, and its weight subtracted from the weight of the plaster taken. This gives the weight of the compound used.

The mixed solutions of the compound, measuring about 200 c.c., are now well stirred and then allowed to stand covered in a tall

beaker until all the gray metallic mercury has settled to the bottom. This usually is accomplished in about twenty-four hours. Chloroform can be substituted for benzol in this dissolving operation, but benzol is used in our work on account of its relative lightness, because of which the mercury settles more quickly.

When the gray mercury has settled out pour off carefully the supernatant benzol which contains the rubber and resins in solution. On account of the high gravity of the mercury the benzol can be decanted until nothing remains but a slime of mercury powder. To this add at once one or two c.c. of aqua regia, warm it, stir, and let stand. If all gray color is not removed in about an hour add another c.c. of aqua regia, stir, warm, and let stand again, repeating the operation, if necessary, to dissolve all of the mercury. Use, however, as little acid as possible so as to avoid all but a slight excess, for much excess will interfere with the subsequent precipitation of the mercury by means of  $H_2S$ . When the acid solution has lost all gray color, indicating the complete solution of the mercury, add about 50 c.c. water. Stir, and filter through a paper filter containing a tuft of absorbent cotton. The cotton catches the flocculent particles of resinous matter and prevents stoppage of the filtration by clogging. Rinse out the beaker with repeated portions of water, which is poured through the filter. Continue until about 200 c.c. of filtrate is secured. Place this filtrate in an Erlenmeyer flask of ample capacity, pass  $H_2S$  through it until the mercury is all precipitated as black  $HgS$ . Let it settle a few minutes and filter at once through a weighed filter paper of fine texture, wash the precipitate on the filter with a little water and dry at  $100^\circ C.$ , cool, and weigh. Subtract the weight of the filter paper and calculate the resultant weight of the mercury sulphide to mercury, viz.:

$$232:200 = \text{wt. } HgS : x \text{ wt. mercury.}$$

The weight of mercury found multiplied by 100 and divided by the weight of the compound used gives the per cent. of mercury in the compound.

#### AMMONIAC AND MERCURY PLASTER.

The requirement of the U.S.P. is that this plaster shall contain 18 per cent. metallic mercury.

*Method of Assay for Mercury.*—This is the same as with mercurial plaster.

## STRENGTHENING PLASTER.

*Assay for Iron.*—Weigh out accurately two pieces of plaster of about 5 Gm. each, cutting them side by side from the same piece in order that the relative amount of compound to cloth will be the same in each piece.

Dissolve off the compound from one of the pieces with repeated portions of chloroform until the cloth is clean. Allow the cloth to dry spontaneously and weigh it. Multiply its weight by 100 and divide by the total weight of plaster used. This gives the per cent. of cloth in the plaster, the figure so obtained to be used later.

The second piece of plaster of known exact weight is placed in small clippings in a porcelain crucible and ignited. Dissolve the residue in warm concentrated hydrochloric acid, dilute to about 200 c.c. with water, and filter. Pour the solution into a porcelain dish, heat nearly to boiling, and add ammonia in excess to precipitate the iron as  $\text{Fe}_2\text{OH}_6$ . Allow the precipitate to settle, decant on to a paper filter of known low ash value, wash the precipitate with hot water, and dry. This is now ignited in a weighed porcelain crucible with lid, the iron hydroxide being first carefully scraped from the filter and ignited alone in the crucible and the paper containing only a little adherent hydroxide is ignited separately on the lid of the crucible. When the paper is completely reduced to ashes, the lid is placed on the crucible and both are transferred to a desiccator to cool. When cooled, weigh and subtract the weight of the crucible and lid from the weight of the same with contents. This gives the weight of iron oxide ( $\text{Fe}_2\text{O}_3$ ) contained in the crucible.

This is calculated to metallic iron, viz.:

$$160 : 112 = \text{wt. } \text{Fe}_2\text{O}_3 : x \text{ wt. Fe.}$$

The percentage of cloth in the plaster has been determined as above in other piece of plaster, therefore the weight of the piece of plaster ignited is multiplied by the per cent. figure for cloth, determined in the other piece of plaster. The weight so found is subtracted from the weight of plaster ignited, which result is the weight of compound ignited.

The weight of Fe found, multiplied by 100, and divided by the weight of compound ignited gives the per cent. of Fe in the compound.

To Arthur W. Clark and Powell Hampton acknowledgment is due for work in the elaboration of these processes.



# THE CHEMICAL ASSAY OF FLUIDEXTRACT OF ERGOT.

BY JOHN R. RIPPETOE.

Dr. Horatio C. Wood, Jr., has recently shown (AM. JOUR. PHARM., 81, p. 215, May, 1909) that the benzol extract of the fluid-extract of ergot bears a proportional relation to its physiological action. Dr. Wood's physiological tests were made by the blood-pressure method.

The writer for the past three years has been testing the fluid-extract by observing the action upon the cock's comb. Although the method is considered by most workers to be of little value, a marked difference is noted between fresh and old preparations. A fluidextract made from a drug of good quality, when injected into the thigh muscle of a Plymouth Rock rooster in a dose of 1.5 c.c. to one kilogramme bodyweight of rooster produces characteristic physiological reactions; the breathing is dyspnœic, the wings are drooped, there is stupor, diarrhœa, and the wattles and comb become pale and then bluish-black in color. The dyspnœa usually passes off within three to five hours and the comb becomes normal within six to eight hours. After one year or more the preparation requires a larger dose to produce the same results. Apparently, so far as the action on the rooster is concerned, the preparation has deteriorated.

Some of the preparations tested as above in the past have been recently assayed by Dr. Wood's benzol-extract method, the method having been modified as follows: Introduce 10 c.c. of the fluidextract into an eight-ounce bottle, add 20 c.c. water and 100 c.c. benzol. Shake the mixed liquids in a mechanical shaker for thirty minutes. Allow the liquid to stand until the benzol solution is clear. Decant 50 c.c. of the benzol solution, evaporate, and dry the residue to constant weight on a water-bath at a low temperature.

	Date When Fluidextract Made.	Test on Rooster.		Benzol Extract. Oct. 1909.
		Date.	Result.	
A	June, 1907	July, 1907	Good	0.14 Gm. in 100 c.c.
		Feb., 1908	Poor	
B	Nov., 1907	Feb., 1908	Good	0.20 Gm. in 100 c.c.
		Dec., 1908	Poor	

C	May, 1908	June, 1908	Good	0.26 Gm. in 100 c.c.
		Jan., 1909	Poor	
D	June, 1909	July, 1909	Good	0.55 Gm. in 100 c.c.
Alcoholic-drug extract	Dec., 1908	Good	0.56 per cent.	
Glycerin-drug extract	Dec., 1908	Very poor	0.09 per cent.	

The preparations were considered of "poor" quality when they required a 25 to 50 per cent. increase in the dose to produce the characteristic reaction of a preparation passed as "good." Each preparation was tested in duplicate, using two roosters and using the roosters for only one test. The samples marked alcoholic and glycerin-drug extract, were prepared and used for comparison of alcoholic and glycerin menstruums as reported by me in a paper published in the *AMER. JOUR. PHARM.*, 81, p. 85, Feb., 1909.

While no previous assays of benzol extract were made on the samples, it is of interest to note that they contain a proportional lower amount of extract according to their age. It is also noted that the preparations after eight months' aging required larger doses to produce the desired action upon the cock's comb.

ANALYTICAL DEPARTMENT,

Schieffelin & Co., New York.

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## THE NEW ITALIAN PHARMACOPŒIA.

BY M. I. WILBERT, Washington, D.C.

*Farmacopea Ufficiale del regno d'Italia*, terza edizione, is the official title of the new Italian Pharmacopœia bearing the imprint: "Roma Tipografia delle Mantellate, 1909," and advertised to sell for Lire 5 (about one dollar).

Coming as this book does shortly before the convening of our own Pharmacopœial Revision Convention, a review of some of the more characteristic features may perhaps be of interest as suggestions for innovations to avoid or to adopt.

The book is printed in Italian with Latin sub-titles and contains a total of xiv and 452 pages, 8vo. As a pharmacopœia it contains an innovation in the shape of an "Elenco" containing descriptions of proprietary preparations, including a total of 91

titles; several of these titles, however, include a long line of preparations, such as hypodermic solutions and medicinal granules.

The official descriptions from the "Spirit of Minderer" (*Acetato di Ammonio*) to "Sugar" (*Zucchero*) cover a total of 340 pages and aggregate 659 titles or monographs: 17 animal drugs, 158 vegetable drugs, 195 chemical substances, 257 pharmaceutical preparations, and 18 general descriptions or formulas.

For the student who is not well versed in Italian this book is rather difficult to consult, as it is arranged alphabetically according to the Italian titles.

Thirty titles were deleted and 54 new titles added. Among the new additions we find such old and new friends as acetyl salicylic acid; adrenalin, diethymalonylurea, hexamethylene-tetramine, ether for anæsthesia, silver fluoride, quinine ethylcarbonate, sodium formate, sodium glycerophosphate, calcium glycerophosphate, pyramidon, methyl salicylate, stovaine, talcum, trional, quinine tannate, trioxymethylene, seidlitz powder, and wine of antimony.

The provisions of the International Congress for the unification of the formulæ of potent medicaments are closely adhered to and all of the titles included in the Brussels protocol are designated (F. I.) "formola internazionale." The international drop counter is recognized and a table added giving the number of drops of official preparations necessary to weigh one gramme, also the weight of one drop in milligrammes.

Many of the monographs include two or more drugs, thus under "arnica" we find descriptions of "arnicæ flores et rhizoma" and under "arancia amaro" descriptions of "aurantii amari cortex, flores et folia." The botanical descriptions are general rather than detailed and there are comparatively few tests included in the descriptions for vegetable drugs.

The titles of official preparations are all enumerated under the descriptions of the drugs and chemical substances.

Volatile oils are classified under the general heading "Essenze," "olea volatilila" and the related aromatic waters are directed to be made, by distillation, from the drug itself.

Among the more novel pharmaceutical preparations are granules of aconitine, of arsenous anhydride, of strychnine nitrate, and of atropine sulphate, also ophthalmic discs of atropine, of cocaine, and of eserine.

Under elixirs we find but a single title "elixir acidum hallerii."

a mixture of equal parts, by weight, of concentrated sulphuric acid and 90° alcohol.

Fluidextracts are represented by four formulas—"segata cornuta" (ergot), "hamamelis," "idraste" (hydrastis), and "cascara sagrada."

Decoctions and infusions are still liberally represented. Under the general heading "Decotti-Decocta," we find ten additional formulas and under the general heading "Infusi-Infusa" we find no less than eighteen additional formulas, two of these latter preparations are compound preparations, one practically the equivalent of the aqueous tincture of rhubarb of the N. F. while the other is an infusion of senna with manna.

Under "Sterilizzazione" we find a comprehensive monograph on sterilization, including directions for sterilizing with and without an autoclave and notes directing attention to some of the precautions that are necessary to prevent decomposition of such substances as cocaine, morphine, and eserine.

Maximum single and daily doses are appended to the more potent articles and the preparations containing them and these doses are again presented in the form of a table in the Appendix to the pharmacopœia.

Among the remaining, more or less interesting, tables that are appended we find a list of reagents and volumetric solutions and a list of indispensable chemical apparatus, a list of medicaments that must be in stock, and also a list of the pharmaceutical apparatus that must be in each pharmacy, and finally the protocol of the Brussels Conference for the unification of the formulæ of potent medicaments.

The index is rather a comprehensive one and includes thirty double column, closely printed pages.

In conclusion it may be said that the Italian Pharmacopœia, in common with practically each one of the recently published pharmacopœias of the Latin European countries, is a curious jumble of the old and the new. It represents a survival of antiquated and obsolete drugs and preparations with modern ideals for international standards and an unusually great number of the newer remedies.

It recognizes the value of sterilization and is the only national pharmacopœia to recognize and describe proprietary mixtures. Taken altogether, however, the book is a creditable one indeed and reflects erudition and ability both on the part of the medical practitioners and the pharmacists for whose use it is designed.



## PROGRESS IN PHARMACY.

By M. I. WILBERT, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

Not for many years have the happenings in the pharmaceutical line attracted such wide-spread attention and discussion as at present, and, if interest is an indication of importance, pharmacists who can manage to keep abreast of the progress that is being made are destined to come into their own in the near future.

The interest in the forthcoming Pharmacopœial Convention is growing. Both medical and pharmaceutical journals are devoting considerable space to the consideration of matter relating to the Pharmacopœia. As the time for the convention approaches, we also find an ever-increasing difference of opinion on the scope and content of the Pharmacopœia manifesting itself. One extreme, in this connection, is that embodied in the so-called Coudrey Bill.

*The U.S.P. and the Coudrey Bill.*—Some of the daily papers and many of the medical and pharmaceutical journals have recently devoted considerable space to the discussion of a bill introduced in the House of Representatives on December 10, 1909, by Representative Coudrey. This bill is officially designated as H.R. 13859, and it provides for the amendment of the Pure Food and Drugs Act of 1906 so as to require "That the United States Government should edit and publish the United States Pharmacopœia or the National Formulary, and have a complete test for purity and strength of all drugs and chemicals whether generally used or not."

Dr. H. H. Rusby (*A. Ph. A. Bulletin*, 1910, p. 82) recently expressed the belief that the Pharmacopœia being a national standard should include all drugs that are used to any considerable extent. He also believes that a new class of drug standards will be essential. Such a class should include: ash test, limit of starch in non-starchy drugs, limit of woody tissue in non-woody drugs, extraction constants, and clearer definitions.

*The Medical Profession and the Pharmacopœia.*—An editorial points out that: "A thoroughly up-to-date Pharmacopœia—one which will truly reflect the best medical practice of the present time—will contribute more to sane drug therapeutics than any other

one thing," and quotes Sollmann who suggests that: "If the Pharmacopœia is not and cannot be made practically important to physicians, then let us abandon it altogether."—*J. Am. M. Assoc.*, 1909, 53, p. 1645.

*Suggestions for the Pharmacopœia* of the United States by Dr. Oliver T. Osborne, of Yale Medical School, have appeared in serial form, in recent numbers of the *Journal of the American Medical Association* (1910, 54, pp. 50, 132, 208, 290, 376, 467). The author presents a number of really practical suggestions that are well worth careful consideration, but they are too numerous and too comprehensive to reproduce in abstract.

*The National Formulary*.—This book is also attracting considerable attention, and much valuable material is being presented in connection with the meetings of the local branches of the American Pharmaceutical Association. Among the more novel suggestions offered recently is one offered at the meeting of the Pittsburg Branch of the A. Ph. A. by Louis Emanuel, who proposes the introduction of a class of preparations designated "Vehiculæ" to be used as the name indicates, as vehicles for active medicaments.—*A. Ph. A. Bulletin*, 1910, February, p. 90.

*The National Formulary Superfluous*.—Donald McKesson is quoted as saying: "The N.F. as an official standard in prescribing the make-up of compounds hinders progress and improvement. It is only necessary that the ingredients be standard and the label correct and sufficiently descriptive. It is, of course, understood that some few of these compounds, by reason of popular and long usage, should be controlled and these might be properly introduced into the U.S.P."—*Drug Topics*, 1910, p. 19.

*Digest of comments on the Pharmacopœia* of the United States of America (eighth decennial revision) and the *National Formulary* (third edition) for the calendar year ending December 31, 1906, has just been published as *Hygienic Laboratory Bulletin* No. 58. The book comprises a total of 523 pages and includes a comprehensive review of the literature of 1906 relating to official articles. This bulletin is available to all who may be interested on application to the Surgeon-General of the Public Health and Marine-Hospital Service.

*Reports of the Chemical Laboratory* of the American Medical Association to January 1, 1909, and *Reports of the Council on Pharmacy and Chemistry* for 1905, 1906, 1907, and 1908 are two

small 8vo volumes of 84 and 207 pages respectively that contain much useful and interesting information relating to the composition of medicinal substances and the method of exploiting them. The information contained in these books should be of value to the pharmacist and the pharmaceutical chemist, and the two volumes might very properly find a place on the reference book-shelf of every pharmacy.

Among government publications that contain information of more than usual interest to the pharmacist are *Bulletin No. 61 of the Hygienic Laboratory* and *Bulletin No. 126 of the Bureau of Chemistry*. The former of these bulletins records quantitative pharmacological studies on the relative physiological activity of commercial solutions of epinephrine, by W. H. Schultz, and the latter (see *A. J. P.*, 81, p. 420) contains a compilation of data on the "Harmful Effects of Acetanilid, Antipyrin, and Phenacetin," by L. F. Kebler, F. P. Morgan, and Philip Rupp. The latter bulletin has served to arouse renewed interest in the harmfulness of so-called "patent" medicines generally, and with other happenings of more recent date has served to call renewed attention to the responsibilities of the pharmacist in connection with the exploitation and sale of nostrums.

Up until quite recently it was generally supposed that retail druggists as a class recognized the mischief that could be and was being done by nostrums generally and that the continued sale of these articles in drug stores was at least largely due to the fact that patrons had become accustomed to purchase them, in connection with postage stamps and soda water, in the modern combination emporium known as a drug store. The development of a number of co-operative patent medicine manufacturing concerns has attracted the attention of medical men and the *Journal of the American Medical Association* has but recently (January 8 and 22, 1910) called attention to the methods of one of the larger of these concerns. The several editorials have attracted considerable attention, and in pharmaceutical circles have tended to show the existence of differences of opinion even among men of whom it might have been expected that they would be well informed in regard to the limitations of ready-to-take medicines.

That there are still many retail druggists in this country who are not willing to sacrifice honor for profit is evidenced by the open letter from Mr. Henry C. Blair, published in the *Pharmaceutical*

*Era* (February, 1910, p. 128) and by the reported action of the Philadelphia Association of Retail Druggists disavowing any interest, as an association, in the American Druggists' Syndicate.

*British Pharmaceutical Codex*.—This book, which has been out of print for some months since, is now in press and at a recent meeting of the Council of the Pharmaceutical Society it was announced that proof would soon be ready to submit to the Codex Revision Committee.

*Pharmacopœia Suecica IX*.—A review of the recent, ninth, edition of the Swedish Pharmacopœia calls attention to a number of more or less novel features. It appears that this Pharmacopœia has taken rather an advanced stand regarding active ingredients, and directs that for oil of anise or oil of fennel anethol be dispensed and that for oil of eucalyptus or oil of cajuput, eucalyptol be furnished.—*Apothek.-Ztg.*, Berl., 1910, 25, p. 29.

*New Hungarian Pharmacopœia*.—A review of this, the third, edition of the Hungarian Pharmacopœia points out that the decree of the Minister of the Interior, bearing the imposing number 100,000, specifies that this book become the official authority on January 1, 1910. The book is printed in Magyar and in Latin, the two being bound together in a single volume. The work includes 526 official preparations and 106 reagents. The Latin nomenclature resembles that of the German and Austrian Pharmacopœias and the monographs generally suggest those included in the German Pharmacopœia. The decisions of the Brussels Convention have been closely adhered to and percolation has been generally adopted for preparing the tinctures of potent drugs. Specific gravity and extract content is specified for some tinctures and the alkaloid content is also specified in some instances. The list of appliances and utensils with which every pharmacy must be supplied includes: a distilling plant, a steam apparatus, a tablet machine, a sterilizer, and a compound microscope, magnifying at least 300 diameters.—*Chem. and Drug.*, Lond., 1910, 76, p. 18.

*New Italian Pharmacopœia*.—The "Farmacopea Ufficiale del Regno d'Italia," III, is the first of the Continental pharmacopœias to be re-revised since the meeting of the International Conference in Brussels. It will perhaps be remembered that the second edition of the Italian Pharmacopœia was in press at the time and the Brussels Conference Protocol was therefore included as an appendix. In the present edition the several provisions of the protocol have been



quite fully embodied in the Pharmacopœia itself and each one of the included articles is specially designated (F. I.).

*Centenary of the Journal de Pharmacie.*—The centenary of the universally well known "Journal de Pharmacie et de Chimie, Paris," was recently celebrated by a dinner given at the Palais d'Orsay Hotel by Professor Jungfleisch, president of the Editorial Committee of the journal, to his colleagues. The history of the journal was reviewed and its influence on the evolution of pharmacy in all portions of the world was commented on.—*Chem. and Drug.*, Lond., 1910, 76, p. 37.

*The Transactions of the Section on Pharmacology and Therapeutics* of the American Medical Association, at the sixtieth annual session, held at Atlantic City, N. J., June 8 to 11, 1909, have just been published and constitute a large 8vo volume of 252 pages. Much of the material presented in this volume is of unusual interest to pharmacists, as it includes all of the papers and discussions on the Pharmacopœia that attracted such attention at the time. The book is printed by the American Medical Association Press, Chicago.

*Serums and Vaccines.*—A recent number of the *Journal of the American Medical Association* (Jan. 22, 1910) is devoted largely to a discussion of serums and vaccines, no less than eleven separate communications being included. For two of the preparations, vaccine virus and tetanus antitoxin, the plea is made that they should be included in the next edition of the U.S.P.

*Serotherapy and the Pharmacopœia.*—An editorial, commenting on the above series of papers on sera and allied products, calls attention to the great importance of these substances and the desirability of having a number of them recognized in the Pharmacopœia, with proper directions for their preservation and an enumeration of the precautions that are necessary to guarantee uniform efficiency.—*J. Am. M. Assoc.*, 1910, 54, p. 295.

*Vaccine Virus.*—Dr. M. J. Rosenau believes that vaccine virus is deserving of official recognition because it is the oldest and best known specific preventive. It is a drug in the broadest sense of that term, and official recognition at this time would tend to establish for it an official and legal name and avoid future confusion with the bacterial vaccines and other so-called "vaccines" that are now being used in the prevention and cure of disease. Another advantage would be secured from the calling attention to the need for keeping this preparation in a uniformly cool place.—*Ibid.*, 54, pp. 250-251.

*Tetanus Antitoxin.*—Dr. John F. Anderson describes the commercial preparations of tetanus antitoxin and calls attention to the variations in strength that were found before the general adoption of the American standard for determining the strength of this substance. He believes that this antitoxin is rightfully entitled to be included in future editions of the U.S.P.—*Ibid.*, 54, pp. 253–254.

*Physiological Testing of Ergot Preparations.*—John C. Umney discusses the practicability of establishing a standard for preparations of ergot, and reports that three physiological experts gave widely varying opinions on a sample of fluidextract of ergot prepared from fine bold ergot by the B.P. method.—*Pharm. J., Lond.*, 1909, 73, p. 794.

*Physiological Standardization.*—Alexander Goodall asserts that there is a growing recognition of the necessity for determining the activity and the probable strength of certain potent remedies whose active principles have hitherto successfully eluded the persevering researches of the chemist. Among the drugs that should be tested in this way he mentions squill, digitalis, strophanthus, cannabis indica, suprarenal substance, and ergot.—*Pharm. J., Lond.*, 1910, 74, pp. 112–113.

*Strophanthin.*—Fleishmann ' and Wjasmenski (*Deut. med. Wchenschr.*, 1909, No. 21) report observations on 31 cases of intravenous injections of strophanthin gratus. While this method of administration is pointed out as being remarkably efficient, attention is also called to the fact that much care is necessary in the use of this remedy, as the therapeutic dose is dangerously near the toxic dose. The dose for an adult they give as 0.0005.—*Nouv. Remed.*, 1909, 26, p. 517.

*Digalen.*—Worth Hale reports a comparative study of digalen and concludes that this article is not a uniformly stable preparation. Biologic tests also indicate that digalen is relatively much less potent than corresponding amounts of crystalline digitoxin but is of about the same activity as digitalein.—*J. Am. M. Assoc.*, 1910, 54, pp. 35–38.

*Digipuratum.*—The same investigator also reports a study of the comparative strength of digipuratum, said to be a purified extract of digitalis, and concludes that this preparation is of about the same activity as the strongest digitalis preparations on the market, but that it appears to offer no special advantages over standardized official preparations.—*Ibid.*, 54, pp. 129–130.

*Colocynth Constituents.*—Power and Moore review the literature relating to the constituents of colocynth and report a comprehensive examination of Turkish colocynth. The seed represented 75.5 per cent. of the weight of the peeled fruit. They further demonstrate that the so-called colocynthin and colocynthitin, and perhaps other products heretofore obtained from colocynth and to which specific names have been attached, are indefinite mixtures, that the amount of glucosidic substance present in this drug is very small, and that the activity of colocynth is due to at least two principles, one of which is alkaloidal, although a very weak base, while the other is non-basic.—*Chem. and Drug.*, Lond., 1910, 76, p. 150.

*Refractive Indices of Essential Oils.*—Ernest J. Parry, commenting on the refractive indices of essential oils, asserts that the refractometer is an absolutely necessary instrument in a laboratory where essential oils are examined, and points out that considerable information regarding the identity and composition of volatile oils can be obtained by the systematic examination of the several fractions obtained in the fractional distillation of an oil. He also enumerates the refractive indices of a number of essential oils, of the normal constituents, of adulterants, and of other liquids.—*Chem. and Drug.*, Lond., 1910, 76, p. 178.

*Cajuput Oil.*—Baker and Smith report that a sample of oil of cajuput distilled from *Melaleuca uncinata* gave: specific gravity 0.9259, optical rotation  $+7.2^\circ$ , refractive index 1.4788, saponification number 3.05, and solubility in 70 per cent. alcohol 1–15.—*Chem. and Drug.*, Lond., 1910, 76, p. 151.

*Medicinal Herbs.*—To pharmacists and others who are interested in the cultivation and gathering of medicinal herbs, an illustrated article in the "Winter issue" of the *Chemist and Druggist* (Lond., 1910, 76, pp. 179–182), describing the cultivation and the gathering of herbs in Kent, will prove to be more than usually interesting.

*Veronal.*—An abstract (from *Medical Press*) points out that an alarming number of deaths from the use of veronal, either by accident or intention, have been reported within the past few weeks, and the matter is pointed out as being well deserving of the serious attention of the government. In a recent veronal poisoning case at Cardiff the coroner expressed the opinion that there should be some legislation which, without interfering with the legitimate trade of the chemist, should form a protection for the public, so

that drugs like veronal could not be so easily obtained.—*Pharm. J.*, Lond., 1909, 83, p. 690.

*Adulterated Squill*.—Karl Dieterich reports sorting over 20 kilos of squill and separating out upward of 1 kilo of fair-sized fragments of stone. This he thinks is too great a proportion to accept as being accidental.—*Pharm. Zentralh.*, 1909, 50, pp. 971-972.

*Echinacea*.—A report of the Council on Pharmacy and Chemistry of the American Medical Association reviews the history and the uses of echinaceæ and points out that its use is characterized by an absolute lack of scientific scrutiny of the claims that have been made for it, and that until more reliable evidence is presented in its favor it is unworthy of consideration.—*J. Am. M. Assoc.*, 1909, 53, p. 1836.

*Sugar Production*.—An abstract from the Board of Trade Journal gives the total sugar production of Europe during the season 1908-9 as being 6,487,000 metric tons as compared with 6,562,274 metric tons in 1907-8. The production of sugar in extra European countries is estimated at 7,765,500 metric tons, thus making a total sugar production for 1908-9 about 14,252,500 metric tons as compared with 13,911,655 metric tons in 1907-8.—*Pharm. J.*, Lond., 1909, 83, p. 690.

*Hydrogen Dioxide*.—Endemann (*Annales de chimie analytique*) remarks that the acidity of this substance, when titrated with sodium hydrate, using phenolphthalein as an indicator, will vary with the age of the preparation. According to his observations the addition of sodium hydrate to an active solution of hydrogen dioxide tends to form NaOOH which does not give an alkaline reaction with the phenolphthalein. To obtain exact results he proposes adding an excess of alkali, heating to decompose the peroxide, and, after cooling, titrating back with solution of hydrochloric acid.—*J. de Pharm. d'Anvers.*, 1909, 65, p. 863.

*Gelatin, Sterilized Solutions of*.—George P. Forrester points out that the possibility of gelatines harboring tetanus spores makes the preparation and use of solutions of gelatin a source of anxiety to the manufacturer and the physician. He outlines several methods for preparing solution of gelatin, including that of the Swiss Pharmacopœia, which provides for controlling the sterility of solutions of gelatin by injecting them into guinea-pigs and white mice.—*Pharm. J.*, Lond., 1909, 83, p. 794.

*Colors, Odors, and Flavors in Pharmacy*.—These are discussed



by W. Gartside in a short paper in which he makes several practical suggestions. He concludes that for alkaline liquids carmine is a satisfactory red color, while for acids tincture of cudbear is to be preferred. For percolating cudbear he suggests the admixture of 50 per cent. of pine sawdust. For a brown color a solution of ordinary caramel is used, and for yellow he proposes a 4 per cent. tincture of saffron or a hydro-alcoholic solution of annatto. For blue a solution of indigo carmine is suggested, and for green a blending of the yellow with the blue. The suggestions for odors and flavors are also quite practical.—*Pharm. J.*, Lond., 1909, **83**, pp. 757-758.

*Syrup of Wild Cherry*.—Robert R. Hallaway reviews some of the recent literature relating to syrup of wild cherry, outlines a method for determining the hydrocyanic acid content of the bark and the resulting syrup, and concludes that not any of the recently described methods for making syrup of wild cherry extracts all of the available hydrocyanic acid.—*Ibid.*, **83**, p. 798.

*Syrup of Wild Cherry*.—J. C. Umney discusses the uses of syrup of wild cherry and points out that this preparation is largely employed as a vehicle for alkaloids such as heroin and codeine, and that these substances are naturally precipitated by the astringent syrup. He suggests that this difficulty might be overcome by a proper selection of the bark, and proposes that the Pharmacopœia include tannin limitation tests.—*Ibid.*, **83**, p. 800.

*Opium Alkaloids in Preparations of Opium*.—Van de Kreke and Swart report a comprehensive study to determine the degree of completeness with which morphine, narcotine and codeine are dissolved in making the several official galenical preparations. The opium used contained 14.7 per cent. of morphine, 3.83 per cent. of narcotine and 0.75 per cent. of codeine. Their results indicate that morphine readily goes into solution, either in an aqueous or an alcoholic menstruum, but that narcotine and codeine are but imperfectly dissolved by the former, while they are readily dissolved by an alcoholic menstruum.—*Pharm. Weekbl.*, 1909, pp. 1338-1342.

*Ointments in Collapsible Tubes*.—A rather ingenious contrivance for dispensing ointments in collapsible tubes is described and figured in a recent number of the *Pharmazeutische Zentralhalle* (1909, **50**, pp. 981-982). The essential feature of the scheme is to encase the ointment in impervious paper and to slide the ointment thus encased into the desired tube.

*International Standards.*—A. Schamelhout reports the Second International Congress for the Suppression of Fraud and comments at some length on the agreement reached in connection with the proposed international standards for drugs. Among these several standards are:

*Aconite.*—Dried aconite root should have a minimum of 0.5 per cent. of total alkaloids.

*Aloes.*—Good quality aloes should be at least 60 per cent. soluble in water and not yield more than 1.5 per cent. of ash.

*Asafetida.*—The portion of this drug insoluble in boiling alcohol, 90 per cent., should not exceed more than 50 per cent. of the total weight and the drug should not yield more than 20 per cent. of ash.

*Balsam of tolu* should not yield more than 1 per cent. of ash.

*Benzoin.*—Siam benzoin should not yield more than 2 per cent. of ash and not more than 10 per cent. of material insoluble in ether or alcohol.

*Cantharides* should not yield more than 9 per cent. of ash and should contain at least 0.5 per cent. of cantharidine.

*Coca leaves* should contain at least 0.5 per cent. of alkaloids.

*Digitalis* should be collected from wild growing plants.

*Ergot* should not yield more than 1.5 per cent. of ash and should contain at least 0.1 per cent. of alkaloids.

*Adeps lane* should not contain more than 0.2 per cent. of ash.

*Codliver oil* should have a specific gravity of from 0.920 to 0.930; iodine index, after four hours of contact, not below 140 and not above 170; and a saponification index of from 180 to 195.

*Hydrastis* should contain at least 2 per cent. of alkaloid.

*Lycopodium* should not yield more than 0.5 per cent. of ash.

*Opium* should contain at least 10 per cent. of morphine. When dried to a constant weight, at 60° C., should not lose more than 10 per cent. of weight. It should yield at least 45 per cent. of extract to water, equal to 38 per cent. of dry extract, and should yield not more than 6 per cent. of ash.

*Rhatany* should yield at least 12 per cent. of extract and yield not more than 5 per cent. of ash.

*Scammony, Natural and Extracted.*—Because of the difficulty presented by the selection of a satisfactory definition for scammony it was decided to postpone this for a future congress.—*Bull. Soc. Roy. de Pharm., Bruxelles*, 1909, 53, pp. 321-340.

## BOOK REVIEWS.

FOOD INSPECTION AND ANALYSIS. For the use of Public Analysts, Health Officers, Sanitary Chemists, and Food Economists. By Albert E. Leach, S.B., Chief of the Denver Food and Drug Inspection Laboratory, Bureau of Chemistry, U. S. Department of Agriculture. Second edition, revised and enlarged. New York: John Wiley and Sons, 1909.

It is now five years since the first edition of this valuable work was published. During this time considerable progress has been made in food-control work, both in this country and Europe. The second edition reflects the progress that has been made, in that the changes and improvements have been incorporated in this volume. Of the chapters which have been revised, those treating of the following subjects may be mentioned: meats and meat extracts; flour (including methods for determining the grade and for the detection of bleaching); noodles and Italian pastes; paprika; prepared mustard; tea; coffee; cocoa products (including milk chocolate); ice cream; maple products; honey; oils (including the Polenske number and Bömers phytosterol-acetate test for vegetable oils); distilled liquors and preservatives (notably benzoic acid).

A valuable chapter on flavoring extracts has been introduced, including the examination of the lesser used extracts of almond, peppermint, wintergreen, rose, cassia, and cloves. A new chapter on the refractometer and its application in food analysis is also included. Much of the credit in bringing this new edition up to date is due to Dr. A. L. Winton, Chief of the U. S. Food and Drug Inspection Laboratory at Chicago.

The work comprises 21 chapters, including nearly 1000 pages, and an indication of its completeness may be had from an enumeration of the subjects treated: Food analysis and official control; the laboratory and its equipment; the functions, proximate components and nutritive value of foods; general analytical methods; the microscope in food analysis; the refractometer; milk and milk products; flesh foods; eggs; cereals and their products, legumes, vegetables and fruits; tea, coffee and cocoa; spices; edible oils and fats; sugar and saccharine products; alcoholic beverages; vinegar; artificial food colors; food preservatives; artificial sweeteners; flavoring extracts and their substitutes; and canned and bottled vegetables, relishes and fruit products. The work is illus-

trated with a number of drawings and about 40 plates of photomicrographs of pure and adulterated foods, and adulterants.

This book is indispensable to food and drug analysts, and besides the cause of pure foods will be materially assisted and advanced by its revision at this time. Analysts using this book are spared the trouble of looking up the literature except when some special question arises, and can devote most of their time to the analyses they have in hand. The preparation of the first edition no doubt contributed to the undermining of the health of the author, and while he has the satisfaction of having produced a work that is much appreciated, it will be some years before authors of such works are adequately rewarded.

TEXT-BOOK OF MEDICAL AND PHARMACEUTICAL CHEMISTRY. By Elias H. Bartley, Professor of Chemistry, Toxicology, and Pediatrics in Long Island College Hospital. Seventh revised edition, with ninety illustrations. Philadelphia: P. Blakiston's Son & Co., 1909. \$3.00 net.

While the general character and form of Bartley's Chemistry is retained in the revised edition a number of changes have been made in the parts devoted to organic chemistry and physiological chemistry.

This is one of the best texts on medical and pharmaceutical chemistry published. The manner of presenting the subject is stimulating to the student, and the facts given are selected with a view of their practical application.

THE VEGETABLE PROTEINS. By Thomas B. Osborne, Ph.D., Research Chemist in the Connecticut Agricultural Experiment Station, New Haven, Connecticut. New York: Longmans, Green & Co., 1909.

This is one of the most commendable of the series of monographs on biochemistry being published by Longmans, Green & Co. Ten of these have already appeared, having been written by men who have gained an international reputation through their researches in their respective fields. The present monograph, dealing with vegetable proteins, is indeed welcome. Every student and reader on the subject of vegetable proteins has felt the need of the bringing together and correlating of the results of the various researches in a single volume.



In the present volume Dr. Osborne has devoted a limited space to a discussion of the general chemical and physical properties of the vegetable proteins. In eleven chapters covering about 100 pages, he gives a historical review of the proteins; the occurrence of proteins in the different parts of plants and their characteristics; the isolation and preparation of seed proteins; basic and acid properties of proteins; the solubility, precipitation, denaturing, physical constants, and products of hydrolysis of vegetable proteins; a classification of vegetable proteins; and some physiological relations of vegetable proteins to the animal organism, and the biological relations of seed proteins to one another. The book is enhanced by a very complete bibliography of over 600 references and has a good index.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Revised by W. Harrison Martindale, Ph.D., F.C.S., and W. Wynn Westcott, M.B., Lond., D.P.H. Thirteenth edition. London: H. K. Lewis, 136 Gower Street, W. C., 1908.

This useful volume has undergone a thorough revision, many portions having been entirely rewritten. Among the new features may be mentioned: formalized gelatin as a substitute for colloidions; glyceextracts or glycerin extracts of drugs; the preparation of yellow mercuric oxide ointment; the organic (non-toxic) arsenic compounds; trypsin preparations, etc., etc. A number of new substances are considered. The recent literature has been carefully gone over and everything which is likely to prove of value to the pharmacist has been included.

E. MERCK'S ANNUAL REPORT, or Recent Advances in Pharmaceutical Chemistry and Therapeutics. 1908. Volume XXII. E. Merck, Chemical Works, Darmstadt, 1909.

This valuable annual report contains much information that is not to be found readily in any other publication. The first hundred pages are devoted to a consideration of organotherapy and organo-therapeutic preparations. This presents an exceedingly interesting historical review of the subject, and also contains much of the newer matter relating to the organic preparations obtained from healthy animals. It is the most complete treatment of this subject that we have seen, giving the manner of preparation, physical and chemical properties, and the results of physiological and clinical tests of all

the substances that are used either on man or for experimental purposes.

Nearly 250 pages are taken up in a similar consideration of the results of scientific and clinical study of a large number of drugs and their preparations and of newer chemicals as well.

DIGEST OF COMMENTS ON THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA AND THE NATIONAL FORMULARY for the calendar year ending December 31, 1906. By Murray Galt Motter and Martin I. Wilbert. Washington: Government Printing Office, 1909.

This digest is issued as Bulletin No. 58 of the Hygienic Laboratory of the U. S. Public Health and Marine-Hospital Service, being published under the direction of the Surgeon-General with the approval of the Secretary of the Treasury. This bulletin embodies the second installment of the digest of comments on the U.S.P. VIII and the first digest of comments on the National Formulary (3d edition), this latter feature having been included at the request of the Council of the American Pharmaceutical Association.

The bulletin contains over 500 pages and includes about 5000 concise abstracts of the literature relating to the official articles published during 1906. The matter reviewed represents about 200 publications, including 18 foreign pharmacopœias. It is safe to say that nothing has ever been published which so completely covers the literature relating to the U.S.P. and N.F. for any one year. While the year 1906 will long be memorable in the minds of pharmacists and others by reason of the enactment of the National Food and Drugs Law, it also marked an era in pharmaceutical progress by virtue of the signing of the "Agreement between the United States and Other Powers respecting the Unification of the Pharmacopœial Formulas" by a diplomatic representative of the United States Government. It is, therefore, extremely fortunate that the complete literature for 1906 representing the views and practical results of the work of men engaged in or allied with pharmacy has been made available in the condensed form and admirable manner that it has in the Digest at hand. The abstracts are not only adequate but readable, suggestive, and indeed stimulating.

When the series of bulletins covering the literature up to the present year are all issued, they cannot fail to effect profoundly the practice of pharmacy. Investigations will be more fruitful; writers more careful; practices more modern; standards in the U.S.P. and

N.F. more exact, and drugs and their preparations more uniform and efficient.

Bulletin 58 is free to those interested in its contents, and may be had by application to the Surgeon-General of the Public Health and Marine-Hospital Service.

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## CORRESPONDENCE

### UNITED STATES PHARMACOPŒIAL CONVENTION.

WASHINGTON, D. C., December 17, 1909.

TO THE ORGANIZATIONS AND INSTITUTIONS ENTITLED TO REPRESENTATION IN THE UNITED STATES PHARMACOPŒIAL CONVENTION, 1910:

For the first time in its history, the United States Pharmacopœial Convention will meet, on May 10, 1910, at Washington as a corporate body; it is therefore of the utmost importance that all the legal and constitutional requirements of the corporation be complied with. The response to the request for data, as to date of incorporation and period of continuous operation, has by no means been complete. Numerous requests have been received for credential blanks and forms for the notification of the appointment of delegates, and many of the notifications and credentials now in hand fail to meet the evident requirements of the Constitution and By-Laws of the Convention.

In order to secure uniformity as to these details and to provide that all the requirements of the Constitution be met, the Committee on Credentials and Arrangements has adopted the enclosed form, four copies of which will be sent to each organization or institution which, from information now at hand, is believed to be entitled to representation. These forms should be filled out carefully and completely, particularly with reference to the data as to date of incorporation and period of continuous operation; for it is highly desirable that these data of historical interest be a matter of record in the archives of the corporation, especially with reference to those organizations and institutions which, having been represented in the Convention of 1900, are, by special provision of the Constitution, entitled to representation in the Convention of 1910. One of these forms, after having been duly filled out, signed and sealed, should be sent to the Secretary of the Committee and another, like-

wise duly signed and sealed, should be given to *each* delegate, inasmuch as the By-Laws require that "*Every* delegate shall present his credentials to the Committee on Credentials and Arrangements." When the delegate registers at Washington on May 10, 1910, these latter forms will be exchanged for a registration and identification card. The blank, on the reverse side of the form, is left for notes by the Committee on Credentials and Arrangements or for a transfer of the credentials from the delegate to his alternate.

The Committee on Credentials and Arrangements is confident that, realizing the importance of these legal details of our corporate existence, even those organizations or institutions which may already have notified the Committee of the appointment of delegates, will be ready and willing to comply with this request and send to the Secretary of the Committee the new blanks completely filled out.

As in harmony with, and in further explanation of, Article I, Chapter VIII of the By-Laws, the Committee has decided that it cannot recognize the right of any one individual to represent more than one organization or institution.

Copies of the Constitution and By-Laws may be obtained on application to the Secretary of the Committee.

MURRAY GALT MOTTER, M.D.,  
Secretary.

MINUTES, COMMITTEE ON CREDENTIALS AND ARRANGEMENTS, U.S.P.C.

PHILADELPHIA, PA.,  
HOTEL BELLEVUE-STRATFORD,  
27. XI. 09. 8.15 P.M.

1. The Committee on Credentials and Arrangements, of the United States Pharmacopœial Convention of 1910, was called to order by the Chairman, Dr. Oliver T. Osborne, of New Haven, Connecticut; there were present Messrs. Samuel L. Hilton of Washington, D. C., William L. Cliffe of Philadelphia, Pa., Dr. Horatio C. Wood, Jr., of Philadelphia, Pa., and Dr. J. H. Beal of Scio, Ohio; *ex officio* members: Dr. Henry M. Whelpley, Secretary, U.S.P.C. of St. Louis, Mo., and Dr. Murray Galt Motter, Assistant Secretary, U.S.P.C. of Washington, D. C.

2. On motion of H. M. Whelpley, seconded by J. H. Beal, Dr. Motter was made Secretary of the committee.



3. On motion, Messrs. Hilton and Motter were constituted a Sub-committee on Arrangements, with power.

4. On motion, the Chairman and Secretary were constituted a committee on the preparation of blank forms for the notification of the appointment of delegates, credentials, and identification cards; the suggestion that the form shown should contain an additional line in red ink giving further instructions being approved.

5. S. L. Hilton reported on the local arrangements already effected: hotel headquarters at the New Willard, with provision for general meeting room, committee rooms, lavatories, registration, hotel rates at eighteen different hotels, etc. On motion this report was approved.

6. The question of railroad rates and arrangements was left to the Sub-committee on Arrangements, with the suggestion that a conference be had with the proper officials of the Congress of American Physicians.

7. On the question of the interpretation of the Constitution and By-Laws, the committee holds that the terms of Sections 1 and 2 of Article II of the Constitution are quite explicit and clear in their definition of eligibility to membership in the Convention.

(a) The word "corporation" in Section 2, Article II, of the Constitution is interpreted to mean the Convention.

(b) The words "examined and acted upon as provided for by the By-Laws," mean certification to the Convention by the Committee on Credentials and Arrangements and the acceptance and approval of this committee's report by the Convention.

(c) The last sentence of Section 2, Article II, is held to be in no sense retroactive and to refer to the Convention of 1910 and Conventions thereafter.

(d) In order further to clarify the meaning of Article I, Chapter VIII of the By-Laws, particularly the last sentence, on motion of J. H. Beal, seconded by S. L. Hilton, the committee decided that it could not recognize the right of any one individual to represent more than one organization or institution.

8. On motion of S. L. Hilton, seconded by H. M. Whelpley, the list of organizations represented in the Convention of 1900, as printed in the U.S.P. VIII, is held to be authentic.

9. On motion of H. M. Whelpley the Secretary was requested to prepare the minutes of this meeting and a statement of such data as it might be advisable to publish which, after approval by the Chair-

man, are to be furnished to the medical and pharmaceutical press.

10. On motion of H. M. Whelpley, seconded by J. H. Beal, it was ordered that the list of delegates to be submitted to the Convention be published, in so far as it may then be completed, on April 1, 1910, with the explicit statement that such publication does not of necessity mean that such delegates will be received and seated by the Convention.

11. There being no further business, the Committee, on motion of S. L. Hilton, seconded by J. H. Beal, adjourned.

Attest: MURRAY GALT MOTTER,  
Secretary.

#### AMENDMENTS TO THE CONSTITUTION.

WASHINGTON, D. C., Feb. 10, 1910.

#### TO THE MEDICAL AND PHARMACEUTICAL PRESS:

At a regular meeting of the Board of Trustees of the United States Pharmacopœial Convention held at Columbus, Ohio, January 28 and 29, 1910, it was resolved, five members of the Board of Trustees assenting thereto, to submit to the next meeting of the United States Pharmacopœial Convention (Incorporated) the following propositions to amend the Constitution of the Convention in the following particulars:

I. To amend Section 2, Article II, relating to membership, by inserting after the title "the Surgeon-General of the United States Marine-Hospital Service," the following: "the Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Association of State and National Food and Dairy Department, the National Wholesale Druggists' Association, and the National Dental Association."

II. Also to amend said Section 2, Article II, by changing the words "three delegates" in line eleven (page seven of the reprint of the Constitution and By-Laws of 1909) to "one delegate"; the effect of this change being to reduce the representation of each organized body and department to one delegate each.

III. Also to amend Article IV, concerning "Committees and Trustees," by changing the title "Committee of Revision," to that of "General Committee of Revision" (*Ibid.*, last line).

The Constitution does not require notice to be given of proposed changes in the By-Laws of the Convention, but to make

clear the purpose of the change proposed in the present title of the Committee of Revision it is hereby announced that the Board of Trustees will submit to the Convention propositions to amend the By-Laws as follows: to increase the number of members on the Committee of Revision, hereafter to be known as the "General Committee of Revision," from twenty-five to fifty, said General Committee of Revision to create from its own membership an Executive Committee of Revision of fifteen members, to have immediate charge of the work of revision, and also giving to said General Committee of Revision certain advisory and supervisory powers over the work of the Executive Committee of Revision.

MURRAY GALT MOTTER,  
Secretary.

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## PHILADELPHIA COLLEGE OF PHARMACY.

### SPECIAL LECTURES FOR 1909-1910.

THE TYPHOID ORGANISM AND ITS RELATION TO THE PUBLIC HEALTH.—Dr. A. C. Abbott, Director of the Laboratory of Hygiene; University of Pennsylvania, gave the fourth lecture of the course on Friday, November 19, at 3.30 P.M., his subject being "The Typhoid Organism and its Relation to the Public Health." The speaker was introduced by Mr. M. I. Wilbert, who remarked on the importance which is coming to be attached to the question of the economic value of health, and spoke of the fact that Dr. Abbott is a former student and follower of Dr. William H. Welch, one of the greatest minds devoted to medicine in the world.

Dr. Abbott's address furnished an excellent résumé of the subject.

He stated that typhoid fever should be of peculiar interest to Philadelphians for two reasons especially:

First, that it was in Philadelphia that a Philadelphia physician, Dr. Gerhard, demonstrated in 1836 that it was a distinct disease from typhus fever, with which it had heretofore been confused, and made it clear to the medical world that typhoid fever must be regarded as a pathologic entity. This demonstration was made in the Philadelphia Hospital.

Second, that by the adoption of common-sense methods, thor-

oughly grounded in scientific investigation, it has been demonstrated in Philadelphia that typhoid fever may be practically eliminated as a serious disease of the people.

During the interval between these two discoveries practically all of our knowledge on this interesting subject has evolved, and it may be stated that the most important of our knowledge concerning prevention began with the discovery of the cause of the disease by Eberth in the year 1880. Following Eberth's discovery the great difficulty that was encountered was in the identification of the organisms that he claimed to be specifically answerable for typhoid fever, and this difficulty was not by any means lessened through the subsequent discovery of an organism in the intestinal canal that is in many particulars so like the typhoid germ as to make their separation more or less uncertain with the methods available at that time. This organism, the colon bacillus, has nothing to do, in so far as is known, with typhoid fever. It was pointed out that while these two organisms are not identical, yet botanically they have a close relation, and more recent studies have shown that there are thirty or forty organisms belonging to the typhoid-colon group which have been modified by their environment, as in the body of man, in culture media, and elsewhere. Dr. Abbott stated that no one, however skilled he may be, can identify the typhoid bacillus by means of the microscope alone, it being a simple rod-shaped organism like others of the group. The various attempts made with the object of devising methods for differentiating the *Bacillus typhosus* were described. Of these the agglutination test, which is based upon the condition that when an individual suffers from an infectious disease he becomes more or less immune to it, is the most reliable. Thus, if a beef-tea culture of typhoid bacilli, in which the organisms are in a motile condition, be added to the blood-serum of a person who has, or has had, typhoid fever, the organisms become immotile and massed together,—agglutinated,—while with a similar culture of the colon organism no such effect is produced. Dr. Abbott said that in the treatment of typhoid fever it is not possible to employ an anti-toxic serum for the reason that the toxin is endotoxic, that is, closely bound up with the protoplasm of the cell (organism), and is only liberated when the latter is broken down, as in the digestion of the organisms by the leucocytes.

Then coming to the more practical side of the subject, Dr.



Abbott said that in order to ward off the disease it is necessary to have a knowledge of the manner of entrance and exit of the germs. He said that they are eliminated both in the feces and urine, and that in many instances the urine of convalescents will show the presence of the bacilli, and that in a few well-authenticated cases the germs continued to be eliminated by the bowels throughout the remainder of the life of the individual, this period extending to forty years in one instance. The control of such cases offers considerable difficulty, but measures are being considered for looking after these so-called typhoid-carriers. It was stated that in order to contract typhoid fever the living germs must gain access to the alimentary canal, and in this connection it was pointed out that personal contact, such as handling a patient, may be sufficient to communicate the disease, and that the number of so-called personal-contact cases is larger than is usually suspected. As is well known contaminated drinking water and foods are also a source of the disease. Dr. Abbott said that when the outbreak of the disease is general, the water supply is usually the source of infection, and when it is restricted to certain areas or districts, as of a city, the milk supply may be suspected. Oysters were likewise mentioned as a source of the disease, and garden vegetables grown near cities on land fertilized with soil taken from the city were also considered to be a probable source of the disease. The house fly as one of the carriers of the disease received a share of attention. In all these instances infection is due to the direct or indirect transferral of the germs from human excreta, it being established that they are not propagated in the bodies of any of the lower animals mentioned. Thus, while the fly and the oyster may be carriers of the germs, they are not themselves the source of infection.

Dr. Abbott said that knowing the manner of elimination of the germs and the manner in which they are communicated, the methods of preventing infection readily suggest themselves. He said that those having the care of typhoid patients might look upon it as a safe rule that every time they place their hands upon the patient the hands became infected, and should be washed with soap and water. Another good rule is to cook all food, including milk, the statement being made that in many other countries milk is invariably cooked before being consumed. The necessity of thoroughly investigating the milk supply was emphasized, as milk is a good culture medium for the organism. Municipal cleanliness and a good water supply

were advocated as a matter of course. Still another method was suggested for combating the disease, namely, vaccination, and statistics were cited showing that where vaccination has been tried, as among the British soldiers in South Africa, Egypt, and India, the number of cases contracted was notably less, and that the mortality among the patients who were vaccinated was about half as great as among those not vaccinated.

Speaking of local conditions, Dr. Abbott said that before the filtration system was introduced for purifying the water supply of Philadelphia the annual number of cases of typhoid fever averaged about 6000, and in one year ran up to about 9000. With the introduction of filtration the number has been reduced about 80 per cent., the remaining 20 per cent. being due to infection from other sources, including the cases of summer vacationists who have contracted the disease elsewhere. During August, September, and October, about 50 per cent. of our cases are traced to outside sources of infection.

With regard to the determination of the presence of typhoid organisms in water supplies, Dr. Abbott stated that the time required for the disease to manifest itself after infection is about three weeks, and that as the germ does not live long in water it is usually not present when examinations are made, and that it is much better to judge of the situation by a direct examination of the surroundings. He said with reference to the inferential test that when the colon organism is found in water the presence of the typhoid organism is indicated, that too much reliance could not be placed upon it, as the colon organism is found in the intestinal tract of all domestic animals, and as these do not suffer from typhoid fever the colon organism is likely to be found in places where the typhoid germs are not present, and that the fact of the presence of the colon organism must be considered along with other available data.

F. Y.

THE MANUFACTURE AND TESTING OF MEDICINAL PLASTERS was the subject of an illustrated address given on Friday, December 10, at 3.30 P.M., by F. B. Kilmer, chemist for Messrs. Johnson & Johnson, of New Brunswick, N. J., one part of which appears in this issue (p. 112) and the remainder of which will be published in a later number of this JOURNAL. The speaker was introduced by Mr. Warren H. Poley, a member of the Lecture Committee, who recounted some of his earlier experiences in the handling and spread-

ing of plasters. At the close of the lecture Prof. Joseph P. Remington thanked Mr. Kilmer on behalf of the College and the classes, stating that he had always found him willing to give information on any subject with which he was familiar. Among the visitors in attendance were Dr. John F. Hancock, of Baltimore, and Mr. Otto Raubenheimer, of Brooklyn. F. Y.

TRYPANOSOMES AND TRYPANOSOMIASES (the Sleeping Disease and its Causes).—The foregoing was the subject of the sixth lecture, which was delivered on Friday, December 17, by Dr. Leonard G. Rowntree, instructor in pharmacology and experimental therapeutics at Johns Hopkins University. The lecturer was introduced by George M. Beringer, who said that the committee had chosen rather a wide range of subjects for this series of lectures, believing that the pharmacist should know something more than pertains directly to his calling.

Dr. Rowntree stated that in both Germany and England commissions had been appointed to consider the problems involved in the cure and control of the diseases due to trypanosomes, while in this country the subject has been taken up by the universities. The trypanosomes are microscopic parasites belonging to that branch of the animal kingdom known as Protozoa, and the diseases set up by the pathogenic forms of this group are known as trypanosomiasis. A number of species of this protozoon has been described, the organisms varying from 24 to 75 microns in length. They are characterized by the presence of a nucleus, a centrosome, chromatic granules, and a flagellum. They are very active, having several movements, and reproduce by division, starting at the centrosome. They derive their nutrition by osmosis, and multiply very rapidly, an infected animal showing the presence of millions of the organisms in a few hours, as in the case of the rat. In 1841 the first trypanosome was described, and in 1901 Dutton found a patient in Gambia whose blood showed the presence of a trypanosome, which was later proven by Castellani, Bruce, Nabarro, and Low to be the cause of the sleeping sickness. Dr. Rowntree described some six diseases which affect the lower animals due to different species of trypanosomes: (1) one, *Tryp. Lewisii*, affecting rats in all countries, including America; (2) a disease in Africa, *nagana*, in the communication of which the tsetse-fly plays a part and which affects cattle, horses, and dogs, but not man, and is supposed to have come originally from wild animals as alligators and rhinoceri; (3) a disease in India,

known as *surra*, affecting horses and camels, the latter being more resistant to the disease and carrying it over from one season to another; (4) a disease affecting horses in South America due to an organism communicated by flies and supposed to have been brought originally from an island at the mouth of the Amazon, a large rodent or rat probably having been the original host; (5) another disease, *Dourine*, affecting horses in Africa and first found in Europe along the Mediterranean coast, and which at one time reached this country, it being found among the horses in Wyoming and one of the Dakotas; (6) still another disease affecting cattle in South Africa, one peculiarity of which is that the native-born cattle are immune to a certain extent.

Then, referring more especially to sleeping sickness, Dr. Rowntree stated that in 1803, just 100 years before the finding of the organism causing the disease, Winterbottom described it as it occurs among the colored people in Africa. He said that the centre of infection extends from Lake Nyanza up to the Nile and over to the Congo, where 73 per cent. of the population has been wiped out. In Uganda some 500,000 of the inhabitants died from the disease in the past five or six years. In describing the course of the disease, Dr. Rowntree stated that it is at first exceedingly insidious, and that one fly (*Glossina palpalis*) constitutes the intermediate host. The disease seems to have a predilection for the nervous and lymphatic systems, and the organisms have been found in the fluid of the lymph-glands and in the cerebrospinal fluid.

Up to the present time arsenic has played the most important part in the treatment of all of these diseases. Both its inorganic compounds and organic derivatives are used, as arsenic trioxide, arsenites, Donovan's solution, atoxyl (sodium p-aminophenyl arsonate). The idea in the treatment of trypanosomiasis is to administer a remedy which is taken up more readily by the parasite than by the host, as suggested by Thomas, and Ehrlich has found that arsacetin (an acetyl derivative of atoxyl) is 1500 times less toxic to the affected organism than arsenic itself. Another compound recently tried by Ehrlich which promises well is phenyl-arsene-glycine, though, as stated by Dr. Rowntree, it is yet far from ideal. Among the other remedies which have been tried are trypan red and other dyes, such as malachite green, and preparations of mercury and antimony. To Koch also belongs much credit for the



knowledge gained in the treatment of this disease, he having gone to Africa to study it at first hand.

The European has been found to be susceptible to the disease as well as the negro, and along the shores of Lake Victoria-Nyanza the governments are co-operating with a view of stamping it out, having already adopted certain restrictive or quarantine-like measures. The disease furnishes three points of attack, namely, the patient, the fly and the organism (trypanosome). F. Y.

PLANTS INJURIOUS TO ANIMALS formed the title of the seventh lecture of the series, which was delivered on Friday, January 7, at 3:30 P.M., by Dr. C. Dwight Marsh, of the Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., who spoke in place of Dr. Rodney H. True, who was prevented from being present. Dr. C. A. Weidemann presided, and at the close of the address, said, after thanking Dr. Marsh for the information given, that he had gotten a broader view of what the government is doing for the people of this country.

Dr. Marsh said that the government had been engaged in an investigation of the loco-disease, which causes such heavy losses to stockmen on the grazing lands of the Great Plains east of the Rocky Mountains, for some years past. Of the plants causing the disease he mentioned the following: *Zygadenus elegans*, injurious to sheep; the larkspurs or *Delphiniums* causing losses among cattle; and lupines causing losses among sheep and also horses. The attention of the government workers was, however, confined mostly to the two plants, *Aragallus lamberti* and *Astragalus mollissimus*, these causing greater loss than all other poisonous plants combined, and having come to be regarded as the loco-plants par excellence. Both plants belong to the *Leguminosæ*. *Aragallus lamberti*, also commonly known as "rattleweed" or "white loco," has a wide range, extending from Alaska on the north down through the whole grazing region of the Great Plains where it is very abundant. *Astragalus mollissimus* ("purple loco," "woolly loco," or "Texas loco") is more limited in its range.

The word "loco," meaning crazy, is of Spanish origin, and is applied in reference to the peculiar nervous symptoms manifested by the affected animals. Dr. Marsh stated that at the time the government experiments were begun, it had not been definitely determined that the loco-disease was due to the loco-plants, a number

of theories having been advanced as to the cause of the disease, although the evidence, including the results of pharmacological experiments by Dr. Mary G. Day, pointed strongly in this direction. The feeding experiments carried on by the government both under corral conditions and in the open, in which the loco-weeds constituted a part of the food on the one hand and were rigidly excluded on the other, have proved conclusively that the disease is due to loco-plants. The course of the disease, which is characterized by marked nervous symptoms, anæmia, and general debility, was described, as were also experiments in the treatment of the disease. As a result of these experiments it was found that Fowler's solution in daily doses of 15 c.c. continued for about one month is the best remedy for locoed horses, and that for cattle daily doses of 0.009 to 0.012 Gm. of strychnine, or daily doses of 0.4 Gm. of sodium cacodylate, given hypodermically, and continued for a period of one or two months constitute the most reliable remedy. It was noted that the locoed animals are especially susceptible to the usual veterinary doses of the medicines named, and hence it was found necessary to administer them in the small doses given. Laxative agents were also found to be an essential feature of the treatment, laxative foods and magnesium sulphate being recommended in this connection.

Dr. Marsh stated that the loco-plants can be destroyed by digging them up, and that this is a feasible practice in some localities.

F. Y.

PHYSIOLOGICAL ASSAY: ITS VALUE AND LIMITATIONS.—This was the subject of the eighth lecture, which was delivered on Friday afternoon, January 21, by Dr. Horatio C. Wood, Jr., associate professor of pharmacology, University of Pennsylvania. The speaker was introduced by Prof. Henry Kraemer who said that there is no subject which should be of more concern to the pharmacist than the efficiency of the preparations which he dispenses, and that therefore every method which promises to be of value, either in the testing of medicines or which will aid in establishing their value, must necessarily be of special interest to him. (See page 101.)

F. Y.

## AMERICAN PHARMACEUTICAL ASSOCIATION.

The officers of the Section on Scientific Papers would again remind you that the annual meeting of the American Pharmaceutical Association to be held in Richmond, Va., the week following May 2, 1910, offers the last and in many respects the most favorable opportunity to discuss matters of scientific interest in connection with the Pharmacopœia of the United States previous to the meeting of the Pharmacopœial Convention to be held in Washington, May 10, 1910.

To insure profitable and comprehensive discussions, it will be necessary to limit the number of communications presented at each session, and, as the sessions themselves are in turn limited, the committee would request that all members of the association who are interested in the work of the Section on Scientific Papers will promptly announce their willingness to contribute to the programme and indicate, approximately, the time that they will require to present their communications.

Communications to be printed in advance of the meeting should be in the hands of the printer at least six weeks in advance of the date of the annual meeting, and titles with the accompanying abstracts to be included on the programme should be in the hands of the Chairman of the Section at least one month in advance of the meeting.

M. I. WILBERT,  
Chairman.

The meeting of the City of Washington Branch of the American Pharmaceutical Association, February 2, 1910, was devoted to a discussion of the report of a special Committee on National Formulary. On motion, the following principles were endorsed:

*Object.*—The National Formulary should be a book of remedies which not only conserve and protect the welfare of the people, but also represent the best that the American Pharmaceutical Association stands for.

*Nomenclature.*—No name should be used which misleads in any particular.

*Standards.*—It is believed that it would be preferable to have a definite standard prescribed, when practicable, for each product recognized.

*Division of Book.*—It is unwise to divide the book into two parts.

*Introductory Notes.*—The National Formulary should include useful introductory notes, comments, etc.

*Metric System.*—The metric system alone should be employed in giving the quantity or proportion to be used in preparing the various products.

*Medicinal Tipples.*—All products which bear any form of stigma characterizing tipples should be eliminated.

*Saccharin.*—The use of saccharin as a sweetening agent for National Formulary products should be discouraged.

*Pills.*—The general direction for making and coating pills should be continued if it is found practicable to present the matter in an intelligible form.

*Artificial Coloring.*—The artificial coloring of official preparations should be discouraged; it is desirable, however, to introduce one or more formulas for preparing coloring solutions to be used when called for by prescriptions.

*Preservatives.*—Preservatives, other than such articles as alcohol and glycerin, should not be used in pharmaceutical preparations.

*Basic Elixirs.*—The introduction of several select basic elixirs is recommended.

*Proprietary Medicines.*—Formulas intended to produce an imitation of some proprietary product should not be included in the National Formulary.

*Supplements.*—Supplements, corrections, and additions should be issued as the progress of pharmacy and medicine may demand.

On motion, it was agreed that the paragraphs endorsed by the members present be submitted to the Committee on National Formulary.

*Saccharin.*—Saccharin was discussed at some length, and it was suggested that because of the wide-spread use of this article and the apparent difference of opinion regarding the possibility of harm resulting from its use, additional information be sought regarding it, and on motion of Mr. Flemer, seconded by Mr. Hynson, the following resolution was adopted.

*Resolved*, by the City of Washington Branch of the American Pharmaceutical Association, that, in view of the extensive use of saccharin and the possibility of harm arising from such use, the matter is referred to the Surgeon-General of the Public Health and Marine-Hospital Service with the request that it be made the subject of pharmacologic investigation.

M. I. WILBERT,  
Secretary.



# THE AMERICAN JOURNAL OF PHARMACY

APRIL, 1910

## IS THERE CARAMELIZATION IN RIVAS'S TEST? \*

BY DAVID WILBUR HORN, PH.D.

The object of this paper is to show that several phenomena accounted for by an *assumption* of caramelization may be accounted for by facts known to many chemists. The paper includes an experimental examination of one case where caramelization had been assumed by way of explanation.

In a paper read some years ago before the Pennsylvania Pharmaceutical Association, W. F. Horn called attention to the fact that when syrup of ferrous iodide has turned brown from age "we can readily restore its original color by boiling it in a flask for a few minutes."<sup>1</sup> J. P. Remington in discussing this point stated that one cannot "decolorize such syrup without the use of animal charcoal, because of the *caramelization*."<sup>2</sup> In a recent paper, West accounted for the appearance of yellow to brown colors on heating glucose broths with sodium hydroxide in Rivas's Test for *B. Coli* by stating that "The sugar is probably *caramelized* by the NaOH." "Lactose solution also becomes yellow to brown, depending on the amount of sugar."<sup>3</sup> More recently, in the discussion of the brownish color

\* Presented at the meeting of the Phila. Section of the Amer. Chem. Soc., Jan. 20, 1910. Reread (by request) at the fifth Pharmaceutical Meeting for 1909-1910 at the Philadelphia College of Pharmacy, Feb. 15, 1910.

<sup>1</sup> Proceedings Penna. Pharm. Assoc., 1903, p. 112.

<sup>2</sup> *Ibid.*, p. 113.

<sup>3</sup> *Amer. Jour. Public Hygiene*, 19, p. 228, 1909. Mr. West's statement was evidently not intended as more than a suggestion, for in a private communication, Feb. 15, 1910, he frankly states that he "has no sure ground to base his assertion on."

of a new, prepared milk, "Monia Milk," at a meeting of the Philadelphia Section of the American Chemical Society, *caramelization* was again resorted to as an explanation.<sup>4</sup>

Caramel is a dark brown substance formed when sugar is strongly heated. The action of heat on cane-sugar may be summarized as follows: When heated, cane-sugar melts at 160° C., approximately. Above its melting point, the sugar becomes colored, and finally changes into a brown mass called caramel.<sup>5</sup> The action of heat produces serious disturbances in the sugar molecule. This has been established since Lipmann observed, in the manufacture of candy, the formation of small quantities of dimethyl furfural, pyrocatechinol, trioxybutyric acid, and trioxyglutaric acid.<sup>6</sup> Stone later proved that acetone is formed simultaneously with caramel.<sup>7</sup>

On glucose, the action of heat is as follows: The ordinary monohydrated glucose,  $C_6H_{12}O_6 + H_2O$ , loses its water gradually and without fusion at temperatures between 50° and 60° C. This dehydration is completed at 80° C. with partial fusion. Anhydrous glucose melts at 144° to 146° C. At 170° C. glucose is transformed into glucosan,  $C_6H_{10}O_5$ , with the loss of one molecule of water. At about 200° C. it darkens and forms a caramel similar to that obtained from cane-sugar.<sup>8</sup>

Caramel then is distinctly a product formed from sugars at elevated temperatures. If it is caramel that is formed at temperatures below the boiling point of water, for example when syrup of ferrous iodide ages at ordinary temperatures or when glucose or milk-sugar is warmed with alkalies as in Rivas's test for *B. Coli*, it would present a case of exceptional interest. I should regard it as hazardous to assert, without experimental proof, that because caramel is a brown decomposition-product of sugar, therefore every brown decomposition-product of sugar is caramel, and every process producing brown colors from sugar is a process of caramelization. By such argument, errors enter the literature of science masquerading as facts, and in direct opposition to the aim of science to eradicate the errors from the data accumulated.

The first experiments to test his assumption of caramelization,

<sup>4</sup> Meeting, Nov. 18, 1909.

<sup>5</sup> Les Sucres et Principaux dérivés, L. Maquenne, Paris, 1900, p. 656.

<sup>6</sup> Ber. Chem. Gesell., Berlin, 26, p. 3057.

<sup>7</sup> Chem. News, 70, p. 117.

<sup>8</sup> L. Maquenne, loc. cit., p. 486.

I made some years ago upon learning of the explanation of the browning of syrup of ferrous iodide. The results simply confirmed the statements of W. F. Horn. The color of the browned syrup vanished quite suddenly when the syrup was heated to boiling. Such evanescence is not a quality associated with the fairly permanent color, caramel.

When I met with the same assumption again recently in connection with Rivas's test, I undertook further experiments that I shall describe.

The first experiment<sup>9</sup> was intended to determine whether or not the formation of a brown color when the glucose broth is heated with sodium hydroxide is dependent on the presence of the peptone, or beef extract with the glucose at the time the alkali acts on it. Accordingly 5 c.c. 10 per cent. NaOH was heated with 0.25 c.c. portions of (a) a 1 per cent. glucose nutrient broth, (b) a similar nutrient broth to which the glucose had not yet been added, and (c) a 1 per cent. solution of glucose in distilled water. The color developed in both tubes containing glucose, but not in the tube of plain nutrient broth. Therefore the other constituents of the broth are not concerned with the formation of the yellow and brown colors.

In order to determine to how great an extent the glucose is involved in the action of the alkali, 45 c.c. of a 1 per cent. solution of glucose heated with 5 c.c. of water, and 45 c.c. of a 1 per cent. solution of glucose heated with 5 c.c. 10 per cent. NaOH, were examined successively in the polariscope. The effect of the alkali, it was found, was to destroy completely the optical activity of the glucose. Evidently, then, all of the glucose is affected by the alkali.

Upon adding sufficient acid to the browned solutions obtained by heating glucose with alkalies, the color immediately disappears.<sup>10</sup> This evanescence resembles that of the brown color in the syrup of ferrous iodide. Is the glucose restored to its original condition when the brown color is destroyed by acids? To answer this question, 49 c.c. of the browned solution described above was treated with 1 c.c. of water, and another 49 c.c. of the same browned solution was treated with 1 c.c. strong sulphuric acid, and the resulting solutions examined in the polariscope. Neither tube showed the

<sup>9</sup> The glucose used in these experiments was crystallized, C.P., monohydrated glucose.

<sup>10</sup> Cf. West, *loc. cit.*, p. 228.

slightest dextro-rotation. The conclusions are that the glucose is seriously involved in the action of the alkali, and that the brown color is the color of a secondary product.

To insure the dissimilarity of the brown color in the glucose solutions to the brown color of caramel, solutions of caramel made by heating glucose at 200° C. for 70 minutes and by adding "caramel brown" used for coloring whiskies to water, were used in the next experiment. Each solution was divided into two parts, one of which was acidified. The color of the acidified solution was then compared with that of the original solution corresponding to it. The acid produced a reduction in the intensity of the colors that was noticeable when a careful comparison was made, but the change was negligible when compared with the entire destruction by acids of the equally intense color of the browned glucose solution.

One of the well known tests for caramel was then selected and applied to the brown solution obtained when glucose is warmed with alkali. I selected Marsh's test as recommended by Crampton and Tolman<sup>11</sup> and used in their extensive researches on the aging of whiskies. The reagent is an emulsion made by adding 3 c.c. of water and 3 c.c. syrupy phosphoric acid to 100 c.c. amyl alcohol. When a whiskey colored with caramel is shaken with twice its volume of this reagent and time is allowed for two distinct layers to form in the liquid, it is found that the lower (aqueous) layer is always colored brown, whereas in the absence of caramel the lower layer is colorless. When, for the purpose of testing my preparation of this reagent, some of it was applied to a "straight whiskey" that I happened to have in my laboratory, the lower layer was colorless. When the browned glucose solution was tested in the same way, the lower layer was brown. Therefore, the test for caramel was positive. It is evident, however, that the results on the browned glucose solution are not comparable with those on the whiskey, for the glucose was alkaline and the whiskey, of course, acid. Accordingly the browned glucose solution was acidified and then tested as before, with the result that the lower layer was now colorless and the same solution that before gave a positive test now gave a negative test, for caramel. Similarly, some of the whiskey was rendered alkaline and then tested. The whiskey that had before given a negative test now gave a strong positive test, showing a brown color in the

<sup>11</sup> *Journ. Amer. Chem. Soc.*, 30, p. 100, 1908.



lower aqueous layer. A fairly large amount of the original whiskey was now treated with the proper amount of Marsh's reagent, and the colorless aqueous layer drawn off by the aid of a separatory funnel. This lower layer immediately became brown when made alkaline, showing that the brown color was due to some substance extracted from the whiskey in the test. These results show the inadequacy of Marsh's test for caramel in alkaline liquids, and they also indicate the direction in which one may look for an explanation of the brown color formed when glucose is heated with alkalis. Before going further in this direction, however, some other experiments should be described.

I tried to obtain spectroscopic evidence of the similarity or dissimilarity of the browned glucose solutions and the solutions of the caramel made by heating glucose at  $200^{\circ}$  C., and the solution of "caramel brown." But none of them showed absorption bands in the visible spectrum, under the conditions of the experiment.

Oxygen gas (from an S. S. White cylinder of compressed oxygen) was then bubbled through the same three solutions. The color of the browned glucose solution began to fade very soon, whereas that of the other two solutions was unchanged. The gas was passed through the solution of the caramel made by heating glucose at  $200^{\circ}$  C. for 15 minutes without effect.

The last experiment performed was intended to test the validity of perhaps the strongest argument for the assumed formation of caramel when glucose solutions are heated with alkalis. These solutions are described in some works on urinalysis as smelling of caramel, especially after they have been acidified.<sup>12</sup> Now it is true that an odor of burnt sugar is frequently associated with caramel, but I failed to find this odor described as one of the properties of purified caramel.<sup>13</sup> Because I noticed that the solutions when hot and acid smelled more strongly than when cold, I subjected such a solution to distillation in a current of steam. The colorless distillate contained the odoriferous substance. I presume one must now abandon as misleading any argument based upon the so-called smell of caramel. It is evident from this one experiment that the

<sup>12</sup> Hammersten, *Physiological Chem.*, Mandel's Translation, N. Y., 1900, p. 80. See "Moore's Test."

<sup>13</sup> Sabanajeff and Antuschewitsch, *J. russ. Chem. Soc.*, 1893, p. 23; L. Maquenne, *loc. cit.*, p. 660.

odor and the color are not inseparably connected, and it is likely that the odor is due to another and colorless substance that may form at the same time caramel is formed, but may also form at other times as well.

The explanation suggested by some of these experiments is that in the browning of the glucose solutions we have to deal with the condensation of glucose molecules. Such condensation is to be expected because glucose is an aldehyde. In the pale yellow color that appears before the brown shades, and that may be preserved for some time by cooling the solution quickly, we may have to deal with an alcoholate or with mixtures of several alcoholates, formed by the action of the alkali on the alcohol groups of the glucose. The experiments with the polariscope suggest that racemization of the glucose molecule may also occur at the time the alkali acts.

Accordingly I examined the literature to see if I could find any ground against these suggestions or any evidence in favor of caramelization. I shall give data from several sources.

When a solution of glucose in absolute alcohol is treated with sodium ethylate, a compound is precipitated which when properly dried is a white to yellow-white powder of the composition  $C_6H_{11}O_6Na$ . When heated to a little over  $70^\circ C.$ , this substance begins to brown and to decompose, even in an atmosphere of hydrogen, with the final formation of a brown, flaky, amorphous mass.<sup>14</sup>

"If an alcoholic caustic-alkali solution is added to an alcoholic solution of glucose, an amorphous precipitate of insoluble alkali compound is formed. On warming this compound it decomposes easily with the formation of a yellowish or brownish color, which is the basis of Moore's Test."<sup>15</sup>

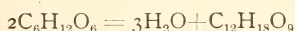
When glucose is heated with water and potassium hydroxide in a loosely stoppered flask on a water-bath at temperatures from  $35^\circ$  to  $40^\circ C.$ , the solution browns after a short time. This color increases in intensity for the first few days, but after some time the liquid becomes colorless. Lactic acid may be isolated from this colorless liquid with a yield of about 41 per cent. Although the rate of this reaction varies greatly with the dilution and the relative concentration of the alkali, lactic acid is always formed and may be separated from the colorless solutions that finally result. Sodium

<sup>14</sup> Honig and Rosenfeld, *Ber. Chem. Gesell.*, Berlin, 10, p. 871, 1877.

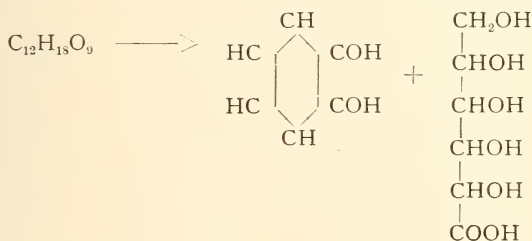
<sup>15</sup> Hammersten-Mandel, p. 80.

hydroxide has exactly the same action as potassium hydroxide. Milk-sugar is also strongly browned by the alkalis, and decomposed with the formation of lactic acid.<sup>16</sup>

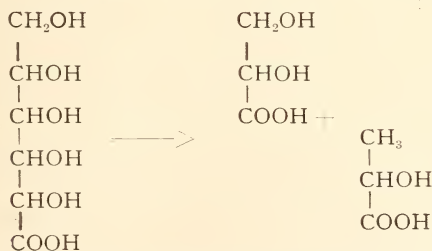
The exact mechanism of these changes has not been worked out, but Gaud<sup>17</sup> has thrown light on parts of the process. He was able to establish the formation of lactic acid, oxybenzoic acid, oxalic acid, and two isomeric dioxyphenylpropionic acids, also "melasique" acid and "glucique" acid constituting the greater part of the "resin" formed when copper oxide is also present with the alkali. These two complex acids had previously been described by Mulder in a paper entitled "Researches on Bodies of a Humus Nature."<sup>18</sup> According to Gaud, some of the glucose undergoes a dehydration and condensation under the action of the alkali with the formation of the complex "glucique" acid,



This acid is unstable and breaks down into pyrocatechinol and gluconic acid:



The gluconic acid separates into glyceric acid and lactic acid:

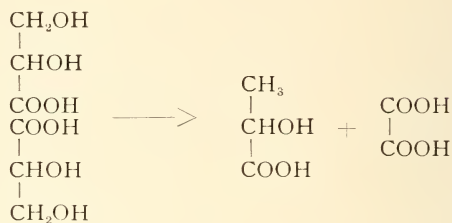


<sup>16</sup> Nencki and Sieber, *Journ. für prak. Chem.* (2), **24**, 498, 1881.

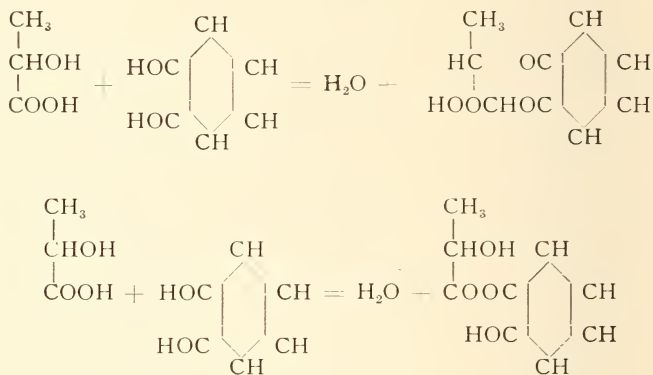
<sup>17</sup> Gaud, *Compt. rend.*, **119**, p. 604, 1894.

<sup>18</sup> Liebig's *Annalen*, **36**, p. 243, 1840.

In the presence of the alkali, the glyceric acid thus formed is transformed into lactic acid and oxalic acid:



Esterification then takes place between the lactic acid and the pyrocatechinol, formed earlier in the process, with the formation of two isomeric esters of hydrocaffeic acid, one of which has acid properties and the other alcoholic properties:



These citations serve to show the complexity of the changes when glucose is heated with alkali, and to suggest the desirability of further work. But they lend no color to the assumption of the formation of caramel, and they do not conflict with the explanation already suggested.

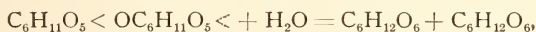
It seems likely that the yellow color developing at first when glucose is heated with an alkali, as in Rivas's Test, is due to some sodium glucose compound of the nature of an alcoholate. On further heating, the major part of the glucose is transformed into lactic acid and other of the organic acids mentioned by Gaud, and part of it is resinified as a result of its aldehyde group. Aldehydes as a class exhibit this latter behavior with alkalies. Thus, if acet-



aldehyde in aqueous solution is warmed with potassium hydroxide, the liquid becomes yellow and after a time reddish-brown amorphous masses are precipitated, "with the simultaneous production of a peculiar odor." The brown substance formed is called "aldehyde-resin."

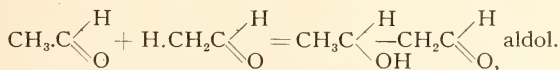
This method of explanation involves no new or improbable ideas. In fact, this behavior of aldehydes is given as characteristic of them, in the usual text-books of organic chemistry.<sup>19</sup> Further, this explanation is consistent with the facts in the case, even supplying some explanation for the bleaching action of molecular oxygen. For aldehyde-compounds would be expected to oxidize. It is also in accordance with the experience of every chemist who has added alkalies to alcohol, before distilling it to free it from aldehydes. The yellow to brown colors produced in alcohol under these conditions are also discharged by acids. And lastly, it explains the formation of a brown color in the almost colorless aqueous layer obtained in Marsh's Test applied to a straight whiskey, when this layer had been separated from the whiskey and then treated with alkali as described in the early part of this paper. For this aqueous layer contains aldehydes.

Milk-sugar gives similar results. An explanation may be found in this case, too, without recourse to the assumption of caramelization. Milk-sugar is well known to be readily hydrolyzed with the destruction of the monocarbonyl bond,



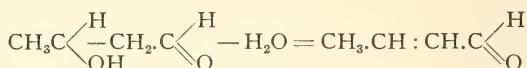
yielding d-glucose and d-galactose. It is also well known that alkalies, or rather hydroxyl ions, catalyze hydrolysis. It may well be, then, that in Rivas's Test the milk-sugar is first partly hydrolyzed into glucose which then reacts with the alkali as suggested above, with the production of the dark colored condensation products.

I do not wish to be understood as omitting the formation of aldols as a part of these condensations. Just as acetaldehyde forms aldol, so other aldehydes may be expected to:

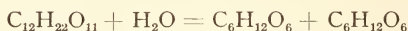


<sup>19</sup> Holleman's *Organic Chemistry*, Tr. by Walker, N.Y., 1906, p. 135; Bernsthen's *Organic Chemistry*, p. 144.

This in no way invalidates the explanation by resinification. For it is probable that aldehyde-resin is a product resulting from the continued condensation of aldol molecules with the elimination of water, just as aldol itself easily loses one molecule of water when heated, with the formation of crotonaldehyde:



In closing, it seems permissible to return to the case of syrup of ferrous iodide. Although we deal here at first with a neutral syrup, it is possible to draw an explanation from the accepted facts of chemistry without recourse to the assumption of caramelization. Ferrous iodide is the salt of a weak base and a strong acid and therefore undergoes hydrolysis with the formation of hydriodic acid and ferrous hydroxide, or basic salts of ferrous iron,  $\text{FeI}_2 + 2\text{H}_2\text{O} = 2\text{HI} + \text{Fe}(\text{OH})_2$ , or basic salts. The fact that this syrup becomes acid as it ages was pointed out by W. F. Horn in the paper already cited.<sup>20</sup> The cane-sugar then would be expected to undergo, at least in part, an *inversion*, or hydrolysis, such as it is well known to undergo in the presence of strong acids such as hydrochloric acid. As to strength, hydriodic acid is to be classed with hydrochloric acid, and it would catalyze this hydrolysis in much the same way as hydrochloric acid. This inversion would likely produce the two hexoses, d-glucose and d-fructose, well known to be produced in the presence of other strong acids:



These two hexoses may then undergo the change which is known as a general reaction for hexoses in the presence of hydrochloric acid, namely, the conversion into levulinic acid,  $\text{CH}_3\text{CO.CH}_2\text{CH}_2\text{COOH}$ , with the simultaneous production of the brown substances known to be produced always in this transformation and called "Humus Substances."<sup>21</sup> Other reactions may occur at the same time,<sup>22</sup> and the browned syrup of ferrous iodide offers an open field for extensive investigation.

<sup>20</sup> Proceedings Penna. Pharm. Assoc., 1903, p. 112.

<sup>21</sup> Holleman-Walker, p. 269.

<sup>22</sup> Cf. W. F. Horn, *loc. cit.*

In fact, the last word, probably cannot be said in any of these cases except after elaborate research, but I believe there is ample evidence that the assumption of caramelization has no adequate experimental basis in the cases discussed, and that it does not even savor of probability, while the alcoholic and aldehydic characters of glucose may well account for the phenomena in so far as they are known at present.

PRIVATE LABORATORY, Bryn Mawr, Pa.

February, 1910.

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## A NOTE ON THE PREPARATION OF CHLORINATED SODA SOLUTION.

BY ELIAS ELVOVE.

The well known method of the U. S. Pharmacopœia (1905) for preparing chlorinated soda solution from chlorinated lime is certainly not a very simple method to say the least. We need only recall the fact that not only is it required to filter the aqueous mixture so as to free it from the insoluble portion remaining in suspension which is frequently a tedious and slow process, but that it is also required to afterwards remove the calcium from the solution by adding a solution of sodium carbonate and filtering off the resulting precipitate, thus involving a second tedious filtration. Again the fact that these precipitates are very bulky and difficult to wash thoroughly renders this process considerably wasteful as well as highly inconvenient when a comparatively large amount of this solution is to be prepared in the ordinary chemical or pharmaceutical laboratory. Also the fact that such preparations, even when kept under the most favorable conditions, are comparatively unstable and hence must frequently be prepared just when wanted, renders the disadvantages mentioned of even greater magnitude than would be the case if this preparation were of a stable character so as not to lose strength on long keeping. Finally, the fact that the chlorinated lime itself is a comparatively unstable substance renders it practically impossible to prepare a chlorinated soda solution of any desired strength, or even with any close degree of approximation, without having to carry out one or more actual determinations of the available chlorine in the resulting solutions.

Recently, a chlorinated soda solution containing about 6 per cent. available chlorine was required in the course of some experiments in the Division of Pathology and Bacteriology of the Hygienic Laboratory and the writer was requested to prepare such a solution. A trial of the present U.S.P. method, using of course proportionately larger quantities of the required substances, showed that this method is inadequate to yield a chlorinated soda solution of such high available chlorine content. The preparation of such a solution by direct passage of chlorine gas into a solution of sodium hydroxide suggested itself, and in looking up the chemical literature on the subject it was found that such a method has actually been employed by Graebe <sup>1</sup> and with very good results. Thus Graebe found that by employing a slight excess of the alkaline solution the stability of the resulting hypochlorite is much increased; for example, if instead of using just sufficient sodium hydroxide to combine with the chlorine, *i.e.*, in the theoretical proportion of  $\text{Cl}_2$  to 2 NaOH, we use these constituents in the proportion of  $\text{Cl}_2$  to  $2\frac{1}{4}$  NaOH, he found that instead of a solution of over 5 per cent. available chlorine losing practically its entire available chlorine at the end of 3 days, it will still show the presence of 5.03 per cent. available chlorine even at the end of 6 days and although the temperature had risen from  $18^\circ \text{C.}$  to  $25^\circ \text{C.}$ , if prepared so as to conform to the latter proportion; while by employing the chlorine and the sodium hydroxide in the proportion of  $\text{Cl}_2$  to 3 NaOH, the resulting hypochlorite solution which immediately after preparation contained 5.7 per cent. available chlorine still showed the presence of 5.37 per cent. available chlorine even after having stood 23 days, during which time the temperature rose from  $18^\circ \text{C.}$  to  $25^\circ \text{C.}$  The effect of light, however, he found unfavorable to its stability and he therefore recommends that such solutions be kept in the dark. Graebe further points out the advantages of the method <sup>2</sup> for preparing chlorine that is based on the reaction between hydrochloric acid and potassium permanganate. Thus owing to the fact that this reaction is practically quantitative it is possible to prepare hypochlorite solutions of definite strengths by using the calculated amounts of the respective substances required. The chlorine thus obtained is also free from chlorine dioxide; and it is possible to carry out the whole process of generating the

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<sup>1</sup> Ber., 35, 2753-2756 (1902).

<sup>2</sup> Ber., 35, 43-45 (1902).



chlorine and forming the hypochlorite solution without noticing the slightest odor of chlorine in the room in which the operation is carried out. About 65 c.c. of hydrochloric acid of sp. gr. 1.17 is required for each portion of 10 Gm. of potassium permanganate used, the evolution of chlorine commencing even without extraneous heating.

A chlorinated soda solution was therefore prepared by Graebe's method as follows: From the proportion

$$70.92 : 120 :: 6 : x = 10.15$$

we see that in order to have the proportion of  $\text{Cl}_2$  to 3 NaOH, the amount of sodium hydroxide should be 10.15 per cent. in the case of a solution that is to contain 6 per cent. available chlorine. For making 500 Gm. of such a solution we will therefore need 50.75 Gm. of NaOH and 30 Gm.  $\text{Cl}_2$  to 419.25 Gm. of water; while on the basis of 10 Gm.  $\text{KMnO}_4$  equals 11 Gm. chlorine, to obtain 30 Gm. of the latter approximately 27.3 Gm. of the former will be required. These respective quantities of the several substances were therefore used in making this solution. The potassium permanganate was placed in a distilling flask of about 300 c.c. capacity, the mouth of which was fitted with a doubly perforated stopper; one of these perforations being used for connecting with the separatory funnel, into which 175 c.c. of strong hydrochloric acid (33 per cent.) was placed; while the other perforation in the stopper was used for uniting by means of suitable tubing the inner atmosphere of the flask with that of the separatory funnel; the latter being an arrangement used by Manchot and Herzog,<sup>3</sup> an illustration of which may also be seen in Loevenhart and Kastle's<sup>4</sup> paper on the catalytic decomposition of hydrogen peroxide. The delivery tube of the flask was connected with a small gas washing bottle (Drexel's), into which was placed about 50 c.c. of water for washing the gas before it passed into the sodium hydroxide solution. The latter was placed in a narrow-mouthed measuring cylinder, which it almost filled, and the gas delivery tube was made long enough to almost reach the bottom of the cylinder. When all the connections had been made, the stop-cock of the separatory funnel was turned so as to let the hydrochloric acid fall slowly in drops on the solid potassium permanganate in the flask. The

<sup>3</sup> *Ann. Chem. (Liebig)*, 316, 321 (1901).

<sup>4</sup> *Amer. Chem. J.*, 29, 397-437 (1903).

evolution of chlorine commences immediately after the acid and permanganate come in contact, and the rate of chlorine generated is easily regulated by the rate of flow of the hydrochloric acid. When the current of chlorine was observed to slow down, gentle heating was applied, and the operation continued until the current of chlorine passing the Drexel washing bottle was observed to have been reduced to just a very slow bubbling. The cylinder and contents were weighed before and after the passage of the current of chlorine and the increase in weight was found to be 29 Gm. This would make the added chlorine represent 5.81 per cent. of the final weight of the solution. An actual determination of the available chlorine in this solution, carried out by the U. S. P. method, showed the presence of 5.80 per cent. available chlorine. This shows therefore that the chlorine value of such a solution may be found by simply determining the increase in weight due to its passage into the solution; and it also shows that perhaps a better plan to follow when a solution of a given chlorine strength is required is to use a little more of the potassium permanganate than would correspond to the formula  $10 \text{ Gm. KMnO}_4 = 11 \text{ Gm. chlorine}$  and determine the increase in the weight of the solution due to the passage of the chlorine into it; when, if the solution is found a little stronger than what is required, it could be diluted to the desired strength by the addition of the calculated amount of the sodium hydroxide solution. It would seem advisable therefore that Graebe's method for the preparation of chlorinated soda solution be adopted in the next revision of the U.S.P.; and perhaps also that the permanganate method for chlorine generation be used in all other pharmacopœial preparations where free chlorine is required, as, for example, in the preparation of chlorine water. This would not only avoid the use of different methods, as the chlorinated lime method for the preparation of chlorinated soda solution and the chlorate method for the preparation of chlorine water, but would also yield other advantages. Thus the latter would then be pure chlorine water instead of as at present containing also the foreign substances, potassium chloride and oxides of chlorine; while "the possible danger arising in the preparation of chlorine from either sodium or potassium chlorate and hydrochloric acid," pointed out by Merk<sup>5</sup> as being due to the decomposition with

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<sup>5</sup> Proc. A. Ph. A., 52, 775 (1904).

explosive violence of the oxides of chlorine which are generated in the chlorate process, would be avoided; also the difficulties pointed out by Shearer,<sup>6</sup> as the impossibility "even under the most favorable conditions, to obtain compound solution of chlorine containing 0.4 per cent. Cl as prepared by the U.S.P. formula," would be overcome; especially, when we remember that in passing the chlorine through distilled water preliminary to its entering the sodium hydroxide solution, we actually obtain in the one operation both chlorine water and chlorinated soda solution. Finally, the fact that the apparatus required is very simple and that it need not occupy much space, as well as the fact that the chlorine is readily generated by simply turning the stop-cock of the separatory funnel so as to allow the strong hydrochloric acid to come in contact with the potassium permanganate, and that the operation can be carried out so as not to notice the slightest odor of chlorine in the room in which this operation is carried out, would seem to offer the additional advantage of permitting the apparatus to be permanently set up and thus kept ready for use whenever free chlorine is wanted; while by also keeping ready for use a supply of the sodium hydroxide solution, the chlorinated soda solution could be prepared in a very short time and with very little attention.

It might be objected, however, that the permanganate method would increase the cost of the chlorine very much. But when we remember that a given weight of potassium permanganate can be used in making more than five times as much chlorinated soda solution as an equal weight of even the best commercially obtainable chlorinated lime, this objection loses much of the force which it might appear at first glance to have. Thus according to an experiment of Arny and Dawson,<sup>7</sup> in which 100 Gm. of chlorinated lime of an available chlorine strength which represented, according to these authors, about the best that is ordinarily obtainable commercially, was used in making 1000 Gm. of chlorinated soda solution by the U.S.P. method, the resulting solution contained only 1.65 per cent. available chlorine; or a total available chlorine of 16.5 Gm., the cost of the chlorinated lime for which would ordinarily be about 2 cents; while on the basis of 27.3 Gm.  $\text{KMnO}_4$  + 175 c.c. hydrochloric acid yielding 29 Gm. available chlorine in the chlorinated

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<sup>6</sup> Proc. A. Ph. A., 55, 669 (1907).

<sup>7</sup> Proc. A. Ph. A., 56, 842 (1908).

soda solution, and taking the average of the quoted wholesale prices for these substances, the cost of even 20 Gm. of such available chlorine need not exceed this amount, thus actually making the permanganate method even slightly cheaper than the present U.S.P. method, even if we do not consider its other advantages. It appears therefore that from whatever standpoint we may view the case the present U.S.P. method for the preparation of chlorinated soda solution is certainly not as advantageous as the method proposed as a substitute.

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Washington, D. C.

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## A NOTE ON CERTAIN COLOR REQUIREMENTS OF THE U. S. PHARMACOPŒIA.

BY NORMAN ROBERTS, M.D.,

Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service,  
Washington, D. C.

Horace North, in Lehn and Fink's "Notes on New Remedies" for January, 1910, objects to the U.S.P. requirement as to the color of turpentine, in that there is no such thing as an absolutely colorless liquid, not even distilled water. This objection is valid, and to meet it definite color-limits should be officially set. The most practicable color standards would probably be dilute solutions of stable and easily obtainable substances, the comparisons being made in large colorless glass bottles or in Nessler tubes—not in test-tubes, since in a tube a flat bottom is necessary to avoid irregular dispersion and consequent inequality of the light.

Thus, in the case of *Oleum Terebinthinæ*, the first requirement should read somewhat as follows:

"A thin liquid, having a characteristic odor; color not more intense than that of a 1: (x) solution of (potassium dichromate) in distilled water, when viewed by diffused daylight transmitted from below, the bodies of liquid compared being one decimetre in depth and contained in similar Nessler cylinders 30 mm. or more in diameter."

Other liquids in the U. S. Pharmacopœia having the same vague



color requirement are as follows: Acetone, the various "colorless" liquid acids, ether, acetic ether, ethyl chloride, alcohol, water and a number of the medicated waters, benzaldehyde, benzin, bromoform, carbon disulphide, cinnamic aldehyde, eucalyptol, glycerin, guaiacol, a number of the liquors, methyl salicylate, oil of peppermint, oil of thyme, spirit of ammonia, spirit of nitroglycerin, terebene.

As no one color standard will do for all these liquids, a number of standards should be provided, and the liquid should be required to be *not more highly colored* than the designated standard, or if a given liquid is found at different times to assume two or more different colors in consequence of various impurities or deteriorations, a corresponding number of color comparisons may be prescribed. For certain of the "colorless" liquids, distilled water itself may serve as the color standard; for others, very dilute solutions of the decomposition products (*e.g.*, for hydriodic acid, iodine), but for most it will be necessary to experiment and find suitable non-related soluble substances by the use of which the usually occurring colors may be matched for practical purposes.

In many, perhaps most cases, a faint color may be present in officially "colorless" liquids, and still the liquid be for practical purposes as good as though it were water-colorless. The Pharmacopœia designedly permits such deviations from absolute perfection as will not result directly or indirectly in injury to the consumer, and will reduce what would otherwise be, in many cases, the prohibitive cost of production. But now that the U. S. Pharmacopœia is a pivotal legal reference work, vagueness of any sort must be eliminated, and all requirements stated in language which shall be, humanly speaking, unmistakable.

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## A NOTE ON CARDAMOM AND OIL OF CARDAMOM.

BY GEORGE M. BERINGER.

At the last annual meeting of the Pennsylvania Pharmaceutical Association the writer contributed formulas for some new basic elixirs that were proposed for introduction in the revision of the National Formulary. Among these was a compound elixir of cardamom in which the oil of cardamom is an essential ingredient. In the discussion following the reading of this paper, some doubt was

expressed as to authentic and pure oil of cardamom being available as an article of commerce and likewise as to its keeping.

These criticisms were not in accord with my own practical experience, as for nearly twenty years I had been using this oil continuously as a flavoring in certain special formulas and had found it very satisfactory, and during all this time I had experienced no difficulty in obtaining a good product nor had I any trouble in keeping it in my oil closet. The change noted in the latter respect was very slight indeed and not at all comparable with changes in such commonly used oils as lemon and orange.

The history of distilled oil of cardamom may be traced back to Valerius Cordus, who first distilled it somewhere about 1540. An oil prepared "by extraction from the seed" as suggested by the critic would be far from satisfactory, and his sample made as described, "by taking the cardamom seeds, grinding them and extracting with a solvent and evaporating the solvent," was probably not more than one-half to one-third pure essential oil, because the fixed oil in this seed is more abundant than the volatile and the ordinary solvents would extract this and leave it in the residue on evaporation.

The writer has always understood the commercial situation to be that a very large portion of the cardamoms harvested are not presentable and will not permit of bleaching either by natural or artificial means. Again part of the fruits become broken or dehisce from over-ripeness. Thus there is always available a relatively large amount of "decorticated" cardamom seeds freed from the almost inert pericarps and very suitable for grinding for manufacturing purposes and for distilling.

However, that there might be no question as to the abundance of a supply of pure oil of cardamom in commerce and that its keeping quality as well as purity might be established before receiving official recognition, further investigation was deemed advisable. The writer addressed a circular letter to a number of the large dealers and manufacturers of essential oils, propounding queries, answers to which would elicit the information desired. Their replies were uniformly prompt and courteous, and they willingly placed at the disposal of the committee data and information concerning the product. I acknowledge my obligation and appreciation of their kindness and am also indebted to Messrs. Dodge & Olcott Co., and the American Branch of Antoine Chiris for gratuitous samples. The object of

the present communication is to submit to the Committee on N.F. an abstract of the information thus obtained and the conclusions which I believe are warranted from these and my own observations.

"The official Malabar and Madras cardamoms are, on account of their high price, hardly ever used for the distillation of the commercial oil which is generally made from Ceylon cardamoms. Also this oil is rather high in price and would, therefore, never be used in larger quantities, so that the demand could probably be filled without difficulty. The keeping qualities of the oil are comparable to those of oil of lemon, orange, etc.

"The available data for testing the purity of the oil are somewhat meagre, and from what I suppose to be its chemical composition it would seem to be not very difficult to adulterate it without altering its various characteristics. Altogether, I would consider it as an article which does not lend itself well to official recognition."—Fritzsche Brothers.

"I am extremely friendly to the article—oil cardamom—knowing its value and worth as a flavoring ingredient.

"*Purity.*—This oil is one that is susceptible to adulteration, and an oil that has suffered tremendously in the past. We believe, however, that, along with other oils of this character, the standard has been raised considerably of late; and at the present time there is no difficulty in securing an oil as an article of commerce that can be officially recognized.

"*Distillation.*—There are several qualities of cardamom seed distilled, but the oils that are in most general use are drawn from the Ceylon and Malabar seed, both yielding a slightly different quality of oil; and in recognizing oil of cardamom, these conditions should be considered. We refer you to Parry and Gildemeister and Hoffmann, who have both analyzed these oils on a number of occasions, and our own laboratory has looked into same frequently.

"*Keeping Qualities.*—In our opinion, from the experience we have had with this article, the keeping qualities are much greater than that of the oil you mention. It is not prone to become terebinthinate and if kept under the ideal conditions that essential oils should be stored we believe it will retain its qualities for an indefinite period.

"*Physical Character.*—This is easily established and any prac-

tical chemist can differentiate between a pure product and an adulterated one; also between the several varieties.

"I would also add that the cultivation of cardamom seed has increased enormously of late, especially in Ceylon, and there will be no trouble in supplying any reasonable quantity that the trade demands."—P. C. Magnus.

"*Oil Cardamom.*—This oil has been sold more or less for medicinal and flavoring purposes, and while we do not know its consumption, we think that it is becoming an article of better demand and should be recognized officially, as it is prepared in sufficient quantities that it can always be obtained. We have not noticed any difference in the keeping quality of this oil and we do not see any reason of any change in the character of this oil or a good many other oils, provided they are absolutely pure.

"The following report of analysis of sample of oil of cardamom of our own distillation is submitted:

" Specific gravity at 15° C. ....	.9378
Specific gravity at 25° C. ....	.9320
Soluble in 4 vol. of 70 per cent. alcohol.	
Optical rotation at 25° C. ....	+ 29° 30'
Saponification number .....	126.5"

—American Branch of Antoine Chiris.

"We have manufactured the article regularly for many years and in relatively a large way, the principal outlet for it being among manufacturers of high grade pharmaceutical preparations who presumably employ it as a flavoring agent in some of their compounded specialties. We do not class it among the especially sensitive oils and are quite certain that we have never had any spoil on our hands, notwithstanding the fact that under favorable conditions in respect of the raw material we sometimes manufacture ahead enough stock to last several years. Your first specific question as to whether the oil is prepared in sufficient quantity to be obtainable at all times we answer positively in the affirmative. We are always in position to supply the article of the very finest quality and in perfect condition.

"Your second question we have already answered substantially and we will add only that oil cardamom cannot be considered in



any sense as being in the same class with oils of lemon and orange in respect of keeping quality. The latter begin to deteriorate almost immediately on exposure, and unless light and air are carefully excluded from them they will become entirely spoiled and worthless in a comparatively short time. Of the cardamom, on the other hand, we have had an open bottle in use for a year or more without any noticeable sign of deterioration.

"Your third question we submitted to Dr. F. D. Dodge, chief chemist at our laboratory and factory, whose reply is as follows:

" 'I have no data as to the keeping quality of the oil, but from the fact that the terpene content is low, would assume that the product was relatively stable.

" 'As to tests: the oils manufactured here have generally agreed with the published descriptions of the Malabar oil. I have found as the result of 14 determinations (1907-1909)

" 'S.G. .933 — .943 at 15° C.  
O.R. + 26° to + 40° at 15° C.

" 'According to some of the German investigators the oil should contain about 45 per cent. of ester, calculated as terpinyl acetate. I have not had occasion to determine this so far, but it could readily be done and, with the other constants, would be of assistance in valuing a sample. But I doubt if chemical tests alone would be sufficient to establish the purity or authenticity of the oil.'"—Dodge & Olcott Co.

"We have manufactured this oil for many years, and our product is used by some of the largest perfumers in France and America. We certainly think it is of sufficient importance to be officially recognized. It is an expensive oil, and therefore the actual weight distilled is not of course very great. We certainly think it is an oil that should be recognized, so as to keep out adulterated oil.

"We have found no trouble with its keeping properties, provided usual and reasonable care is taken not to expose the oil unduly to light and air.

"We think the physical characters and tests for purity can be readily established. In our own case, the raw material (cardamom fruit) we use for distillation is specially selected, not solely on the oil content, but with due regard to the odor value, which, as you

will readily understand, is a very important item in an oil which is used so largely in perfumery. It may interest you if we give you a few particulars of the tests of batches we have done during the last few years. Some of the tests were repeated more than twelve months after the oil was distilled, and the results did not vary appreciably:

## TESTS FROM 1901 TO 1908.

Optical Rotation.	Specific Gravity.	
+ 30.5° .....	0.9474	
+ 12.25° .....	0.9102	Qualities not
+ 12.30° .....	0.9283	used by us. <sup>1</sup>
+ 36.88° .....	0.9315	
.....	0.9291	
.....	0.9330	
.....	0.9293	
.....	0.9322	
.....	0.9300	Sol. in 70% alc.
+ 31.6° .....	0.9349	1 in 4 vol.
+ 32.16° .....	0.9408	1 in 3 vol.
+ 30.6° .....	0.9309	
+ 29.75° .....	0.9302	
.....	0.9305	
+ 39.14° .....	0.9352	1 in 3 vol.
+ 28.00° .....	0.9322	1 in 3 vol.
+ 30.85° .....	0.9347	1 in 3 vol.
+ 31.2° .....	0.9357	1 in 4½ vol.
+ 30.75° .....	0.9349	1 in 4½ vol.
+ 28.25° .....	0.9365	1 in 3 vol.
+ 22.2° .....	0.9314	
+ 22.8° .....	0.9331	1 in 3 vol.
+ 24.35° .....	0.9329	1 in 3 vol.
+ 27.9° .....	0.9335	1 in 3 vol."

—Stafford Allen & Sons, Ltd.

<sup>1</sup> "All our regular oil is distilled from Ceylon fruit.

"In 1901 we distilled a sample of wild cardamoms. These gave us an optical rotation of +12.25 and a specific gravity of 0.9102.

"The same year we tried a sample of Mangalore cardamoms, which gave us a result of optical rotation +12.30 and specific gravity 0.9283."

The latter firm print on their stationery as one of their important specialties "Cardamom Oil," indicating that it assumes a fairly important place in their commercial transactions.

I have recently examined three samples of this oil of different makes, the results being as follows:

	Specific Gravity.	Optical Rotation.	Solubility in 75% Alcohol.	Solubility in 70% Alcohol.
1. . . . .	0.9322	+ 32.6°	2 volumes	3 volumes
2. . . . .	0.9324	+ 29.4°	2 volumes	3 volumes
3. . . . .	0.9323	+ 29.4°	2 volumes	3 volumes

The data before us warrant the following conclusions: that ample supplies of pure oil are available; that it keeps as well as most essential oils and much better than many; that the commercial oil is largely distilled from cultivated Ceylon cardamom as well as from the Malabar; that the specific gravity varies from 0.929 to 0.947; that the oil is markedly dextrogyrous with quite a range running from + 22.2° to + 40°; that oils of lower specific gravity and optical rotation or deficient in flavor are obtained from wild or other cardamoms and must be rejected; that the pure oil is soluble when fresh in three volumes of 70 per cent. alcohol, and after aging somewhat is still soluble in 4 volumes.

The following is submitted as a proposed N.F. standard if the oil be admitted in the revision and follows the style of the U.S.P. VIII.:

#### OLEUM CARDAMOMI—OIL OF CARDAMOM.

A volatile oil distilled from the seeds of *Elettaria Cardamomum* White et Maton (Fam. Zingiberaceæ). It should be kept in well-stoppered amber-colored bottles, in a cool place, protected from light.

A colorless or very pale yellow liquid having the characteristic aromatic, penetrating, and somewhat camphoraceous odor of cardamom and a warm, persistently pungent, and strongly aromatic taste.

Specific gravity 0.924 to 0.947.

Very soluble in alcohol and dissolves readily and clearly in 4 volumes of 70 per cent. alcohol.

It is dextrogyrate, the angle of rotation varying from + 22° to + 40° in a 100 mm. tube, at a temperature of 25° C.

Cardamom and its volatile oil again illustrate the changes that

are continuously taking place in commerce and the need, therefore, of frequent revision of the statements in text-books and accepted authorities regarding the sources of drug products. Only a portion of the cardamom of commerce is now "obtained from the wild plants growing in the Malabar or west coast of India."

Since 1881, the cultivation of *Elettaria Cardamomum* in Ceylon has been very successfully carried on and the quantity of the fruit exported from there has been continually increasing, and the appearance and quality more and more closely simulating the best of the true Malabar product. "Ceylon-Malabar Cardamom" is now an established commercial variety<sup>2</sup> and the "Mysore" variety is likewise initiated and produced on that island. Hence the names heretofore used to designate commercial varieties of cardamoms now become meaningless as designating the countries of growth and export. Parry sums up this situation as follows:

"The majority of the cardamoms of commerce are imported from Ceylon and may be described as 'Ceylon Malabars or Ceylon Mysore,' according as they fit in with descriptions."<sup>3</sup>

Gildemeister and Hoffmann make the unqualified statement that, "The cardamom oil of commerce is not distilled from the official Malabar cardamom from *Elettaria Cardamomum* White et Maton, but from the long Ceylon, the wild growing cardamom of that island, the fruit of *E. major* of Smith, the *E. Cardamomum* var.  $\beta$  of Flückiger. They describe this oil as light yellow, somewhat viscid and having a specific gravity 0.895 to 0.905 and an optical rotation of  $+12^{\circ}$  to  $+15^{\circ}$  and yielding a turbid solution in 70 per cent. alcohol."<sup>4</sup>

They further state "that on account of their high price, the official Malabar and Madras cardamoms from *Elettaria Cardamomum* are seldom used in the manufacture of the volatile oil." They give the characters of the Malabar seed oil, specific gravity 0.933 to 0.943 and optical rotation  $+26^{\circ}$  to  $+34^{\circ} 52'$  and soluble in four and more parts of 70 per cent. alcohol.<sup>5</sup>

E. Parry<sup>6</sup> has examined samples of oils distilled from both

<sup>2</sup> Arzneidrogen, Dr. Heinrich Zornig, Leipzig, 1909, fol. 196.

<sup>3</sup> Parry, Chemistry of Essential Oils and Artificial Perfumes, 1908, fol. 197.

<sup>4</sup> The Volatile Oils, Gildemeister & Hoffmann, translation of E. Kremers, 315.

<sup>5</sup> *Ibid.*, 316.

<sup>6</sup> *Loc. cit.*, 198.



Malabar and Mysore (Ceylon) seeds and reports that there was practically no difference, the result being:

	Sp. gr. at 15.5° C.	Optical Rotation at 16° C. (100 mm. tube).
Oil of Malabar cardamoms. . . . .	0.9418	+ 40° 41'
Oil of Mysore cardamoms. . . . .	0.9418	+ 46° 39'

The wild Ceylon cardamom is not an article of importance nor does it enter commerce in any large amount. In the communication above Messrs. Stafford Allen & Sons state that their experiment with distilling the oil from wild seed was unsatisfactory and they use only the cultivated Ceylon seed for their product, and this is also undoubtedly the practice of the other manufacturers. None of the oils examined showed results comparable with the data reported for wild Ceylon cardamom oil. On the other hand, the reports of Parry, Allen, Dodge, and Chiris as well as my own limited examinations all confirm the statement that the oil now on the market is distilled from the fruit of *Elettaria Cardamomum* and that the statement of Gildemeister and Hoffmann in this respect needs correction.

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## SOLUBILITY OF ALKALOIDS OF CINCHONA BARK AND THEIR SALTS IN WATER AT A TEMPERATURE OF 25° C.

BY GEORGE L. SCHAEFER.

At the request of the editor of the JOURNAL I submit a list of cinchona alkaloids and salts of which the solubility in water at a temperature of 25° C. has been determined.

I desire to call attention to the fact, that some of these salts are partly decomposed by water into a more soluble and a less soluble compound, which property, no doubt, has caused many of the discrepancies in previous determinations, carried out in different ways. For instance, 1 part of a pure basic salt of quinine glycerophosphate of the formula  $(C_{20}H_{24}N_2O_2)_2PO_4H_2.C_3H_7O_2 + 5H_2O$  requires for complete solution about 850 parts of water of 25° C. If, however, a large excess of this salt is treated with water of 25° C. for several hours and frequently shaken, the solution filtered off from the undis-

solved part and tested, the salt will be found of a much greater solubility, requiring even less than 200 parts of water for solution, according to time and quantity used. The remaining undissolved part, when dried and treated again with water in the same proportion and under the same conditions as before, shows further decomposition, but in a lesser degree, and the solution will be found to contain considerably less of the salt than the first solution, and so on. Some others of the salts of cinchona alkaloids act more or less in the same way. Therefore the figures in the appended list show in each case that proportion of water which is required to make a solution with one part of the pure and finely powdered salt, when kept at 25° C. for several days, the mixture being frequently shaken. The results from tests obtained from saturated solutions made with a large excess of the salts or taking the difference between the quantity of the substance used and the weight of the undissolved and dried salt, in many instances, when testing salts of the cinchona group, show too great a solubility of the substances, the solutions containing a more soluble compound than the original salt, leaving undissolved a less soluble residue. The same salts also show a greater solubility when treated with hot water, the mixture allowed to cool off to 25° C., and kept at that temperature for hours to crystallize.

For the determination of the solubility of the pure alkaloids—quinine, cinchonidine, cinchonine and quinidine—I used saturated solutions, which were shaken out with chloroform or ether, as the nature of the alkaloid required, and determined by weight after evaporation of the solvent. The solubility of these alkaloids in water differs greatly, according to age and method of manufacturing. The figures in the appended list are obtained from products made a short time ago, but cannot be used as fixed standards. Other specimens of these alkaloids may be found to be more or less soluble, though chemically perfectly pure, the physical condition and amount of water of crystallization being responsible for the discrepancies. The same can be said of the tannates. Other salts of these alkaloids formed with volatile organic acids also become less soluble by age.

I trust that this paper will be of some use and regret very much not to have the time at present to give more complete figures, including the solubility of cinchona salts and alkaloids in alcohol, ether, etc., the published figures being in many cases incorrect.

The following table gives the amount of water required to dis-

solve one part of the alkaloids of cinchona bark and their salts at a temperature of 25° C.:

	Parts of water required to dissolve 1 pt. of the substance
Quinine alkaloid .....	3000
Quinine acetate .....	50
Quinine anisol .....	2400
Quinine arsenate .....	650
Quinine benzoate .....	360
Quinine bihydrobromide .....	5
Quinine bihydrochloride .....	0.7
Quinine bihydrochloride with urea .....	1
Quinine bisulphate .....	8.5
Quinine chlorhydrosulphate .....	1.3
Quinine chromate .....	3150
Quinine citrate .....	825
Quinine glycerophosphate, basic .....	850
Quinine hydrobromide .....	43
Quinine hydrochloride .....	21
Quinine hydroferrocyanide .....	2000
Quinine hydroiodide .....	205
Quinine hypophosphite .....	35
Quinine lactate, basic .....	6
Quinine nitrate .....	70
Quinine oxalate .....	1400
Quinine phosphate .....	800
Quinine picrate .....	3400
Quinine quinate .....	3.5
Quinine salicylate .....	2100
Quinine sulphate .....	700
Quinine bi-sulpho-guaiacolate (guaiaquin) .....	0.5
Quinine sulpho-phenate .....	250
Quinine urate .....	550
Quinine phenol sulphate .....	680
Quinine tartrate .....	950
Quinine tannate .....	2000
Quinine valerate .....	80
Cinchonidine alkaloid .....	4800
Cinchonidine bisulphate .....	1
Cinchonidine tetrasulphate .....	3

Cinchonidine bihydrobromide .....	7
Cinchonidine hydrobromide .....	60
Cinchonidine hydrochloride .....	21
Cinchonidine bihydrochloride .....	1.6
Cinchonidine salicylate .....	1320
Cinchonidine sulphate .....	92
Cinchonidine tannate .....	1800
Cinchonine alkaloid .....	8800
Cinchonine bisulphate .....	1.5
Cinchonine hydrochloride .....	22
Cinchonine hydrobromide .....	59
Cinchonine bihydrobromide .....	1.8
Cinchonine salicylate (cryst.) .....	590
Cinchonine sulphate .....	85
Cinchonine tannate .....	1100
Cinchonine tartrate .....	32
Quinidine alkaloid .....	6900
Quinidine hydrobromide .....	190
Quinidine hydrochloride .....	86
Quinidine hydroiodide .....	1220
Quinidine salicylate .....	1650
Quinidine sulphate .....	95
Quinidine tannate .....	2100
Quinidine tartrate .....	35
Quinidine bitartrate .....	310

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### THE U.S.P. MELTING POINTS.\*

BY G. A. MENGE, PH.D.,

Division of Pharmacology, Hygienic Laboratory, U. S. Public Health and  
Marine-Hospital Service.

Any one who has had occasion to apply, to any great extent, the various tests prescribed by the U.S.P. will, I believe, agree with me in the assertion that some of them are sorely in need of investigation and standardization. Perhaps to no class of tests does this statement apply more forcibly than to melting points. The chemist

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\* Read before the City of Washington Br. of the A. Ph. A., Mar. 2, 1910.



or pharmacist, although of excellent and broad training, who has not given the subject of melting points some special consideration and study might very reasonably ask, "What are the facts which call for and justify such an investigation?" In answer I would point to the discrepancies, sometimes very marked, that exist between the values published for the melting point of the same compound, as found in various sources of the chemical and pharmaceutical literature. In striking illustration of this fact I would submit data, collected from six different pharmacopœias and the important sources in the literature, upon the two compounds acetanilide and resorcinol: For acetanilide the six pharmacopœias agree within a range of  $1^{\circ}$  ( $113$ – $114^{\circ}$ ), but four different sources in the literature give four different values ranging from  $112$ – $116^{\circ}$ . In the case of resorcinol the values vary from  $109$ – $119^{\circ}$ .

The wide variation in the published melting point values of these two compounds is certainly too great to conveniently hide behind the shield of legitimate "experimental error," yet they are only two of many, more or less similar, examples that might be cited.

In the case of acetanilide the fact that all of the pharmacopœias included in the comparison quote practically the same values for the melting point, also for the boiling point, is very striking but might be misleading. The remarkable concordance often found in the data of different pharmacopœias with reference to a given compound might suggest reliable values, but further study and comparison is apt to lead, first to the suspicion and then to the conviction that it more probably indicates the respect and confidence that the builders or compilers of one pharmacopœia feel toward those of another.

Another striking fact, in answer to the same question, is the protest of pharmaceutical chemists and manufacturers against the melting point standard required by the U.S.P., and the plea for the allowance of a varying margin of several degrees at moderately high temperature above and below that standard; all of which indicates a chaotic condition with regard to melting points that certainly calls for a thorough investigation. And in view of the fact that the U.S.P., through the operation of the Pure Food and Drugs Law, has become a legal standard, and because of the very general use of the melting point as one of its most important tests, it would seem of especial interest and importance to the Pharmacopœia and to all who are in any way connected with it that the

cause or causes of such conflicting values, or of reasonable protests, should be determined and, if possible, eliminated—if not completely, at least to as great a degree as is practicable.

The question naturally arises—"What are the causes of this divergence and what is the remedy?" I would summarize the main causes, though perhaps imperfectly and incompletely, as follows:

1. The great variety of methods used in melting point determinations.
2. Varied individual manipulation, including the so-called "personal factor," and especially the rate of heating.
3. Differences in the physical condition of the compounds.
4. The use of thermometers differing widely in their construction or range, or both.
5. The application or omission of emergent-stem correction and the manner of making it.
6. Widely varying interpretations of just what the melting point is (which might be considered to include the apparent use of decomposition point as equivalent to melting point).

The remedy may be indicated, to a greater or less degree, by a brief discussion under each of these different headings.

A description and detailed discussion of all the methods for melting point determinations that I have so far found described in the literature would doubtless be interesting and instructive but would, I fear, unduly tax not only your patience but also your endurance, and mine. Some of them—designed to eliminate certain specific difficulties in obtaining accurate results—are ingenious, more or less complicated, devices which impress me as being rather fantastic, and impossible of general application.

The methods prescribed by some of the pharmacopœias are, in the main, simple and practical but have not been sufficiently developed, it seems to me, to insure the degree of uniformity in results of which they may be capable.

That the use of different methods constitutes a real cause of divergence in results is, I believe, pretty generally recognized but may perhaps be more emphatically indicated here by citing some very good work in demonstration of this fact.

In 1889 Landolt published the results of a very careful investigation to test the comparative accuracy of several methods, including the determination of the melting points and of the freezing points of compounds with thermometers dipping into the substance;

also various modifications of methods involving the use of capillary tubes (including Piccard's)—using both liquid and air baths; and certain electrolytic methods. These were applied in determining the melting points of three substances (naphthalene, mannite, and anthracene), melting at about  $80^{\circ}$  C.,  $165^{\circ}$  C., and  $200^{\circ}$  C. respectively. *The results obtained for each of these compounds under the same conditions by different methods were variable.*

In 1890 Reissert followed with the publication of somewhat similar work. He used only three methods, all of which were included in Landolt's investigation, but extended his experiments to a much larger number of compounds (24). Here again we find differences in the values obtained for the same compound by different methods—the divergence ranging from a few tenths of a degree at low temperatures to several degrees at high temperatures.

Perhaps the most comprehensive comparative study of different methods that can be found in the literature is that of Tyrer and Levy, published in the Year Book of Pharmacy, 1899 and 1900. In the course of their investigation nine different methods were used, including that described by the British Pharmacopœia, Graebe's, Landolt's, Piccard's, Loewe's, Mill's, Kuhara and Chikashige's, and Levy's acoustical method. Twelve compounds were treated, ranging in melting point from about  $40^{\circ}$  C. to about  $200^{\circ}$  C.

Besides the divergence due to the use of different methods they studied the effect upon the melting point due to varying physical conditions of the compound, to the extent that they determined the melting point of the commercial product, the same dried, and the same purified until there was no further rise in melting point.

The amount of divergence resulting from the use of different methods varied not only with rising temperature but also between different compounds melting at about the same temperature, and ranged from about  $0.5^{\circ}$  at low temperature to about  $3^{\circ}$  or  $4^{\circ}$  at high. With only three compounds, however, was the comparison extended to all nine methods. These compounds were spermaceti, melting at about  $43^{\circ}$ , betanaphthol, at about  $122^{\circ}$ , and picrotoxin, at about  $200^{\circ}$ . The range of divergence in this case extended from about  $2^{\circ}$  for the first two compounds to over  $6^{\circ}$  for picrotoxin. The increase in range of divergence with increase in the number of methods tested upon the same compound under the same conditions is very striking and convincing.

Undoubtedly then the use of different methods is a real and

serious cause of discordant results in melting point determinations. In so far as this cause accounts for divergence in U. S. pharmaceutical practice, the remedy is obviously the adoption by the U.S.P. Committee on Revision of a carefully defined official method.

In an attempt recently made in the Hygienic Laboratory to select or devise a method which could be recommended for such a purpose it was not considered feasible to experimentally test a great variety of methods, nor indeed was such a time consuming procedure necessary, for the specifications laid before us by the Committee on Revision, calling for the utmost simplicity, availability, and economy consistent with reasonable efficiency, made possible the elimination by inspection of practically all methods except one or two which we considered to offer promise. Comparative experimental tests were made upon two methods but the conclusion was soon reached that the simpler—applied with carefully defined procedure—would probably easily meet all practical requirements of pharmaceutical practice and, at the same time, very greatly improve the present standard. This method consists of one of the capillary-tube variety, more or less modified to meet specific conditions as they developed. It involves the use of a simple round-bottom straight glass tube of about 30 mm. internal diameter and about 100 mm. long, flaring slightly at the top like an ordinary test-tube. This tube or container is fitted with a stirring device, which any one can make in a few minutes from a piece of small sized, thick-walled capillary glass tubing of such length that a double bend above the top of the container brings the outer end of the stirrer within easy reaching distance of the hand for convenience in manipulation. When in use the container is filled with a suitable bath to a depth which will permit of such an immersion of the bulb of the thermometer that the upper end of the bulb will be 2 to 3 cm. below the surface of the bath and the lower end of the bulb about equally distant from the bottom of the container.

For melting points up to 150° C.—or even to 180° C.—pure concentrated sulphuric acid was considered the most suitable and satisfactory bath. When fresh it can be used at much higher temperature but then its very irritating fumes make it decidedly objectionable. After much experimentation no bath could be found suitable for work at temperatures much above 200° C. which was not more or less objectionable because of fuming. This difficulty, however, was found to be effectively overcome by a slight modification



of the apparatus, which consisted in fitting the container with a cork, perforated for the thermometer and for the stirrer and with two or three small vents at the edge to avoid excessive pressure. With this modification, a very pure grade of cotton-seed oil, freshly distilled paraffin, certain mineral oils, and a few other substances could be conveniently used up to 300° C. or over; but they soon become colored and have to be frequently renewed. A bath was finally adopted consisting of a mixture of pure concentrated sulphuric acid and potassium sulphate in definite proportions as recommended by Mulliken.<sup>1</sup> In my experience this bath, contrary to the claims made for it, fumes at high temperature almost as badly as the pure sulphuric acid. With the simple cork modification the fumes would char the cork and quickly spoil the bath, but by attaching a disk of thin asbestos to the bottom of the cork and including a glass tube in the perforation for the stirrer both the fuming and the charring were effectively overcome and the bath could be used as high as 350° C., or even to 370° C., with perfect convenience and safety. In all cases where the cork modification was applied the stirrer, in order to avoid inconvenience in attaching the capillary tube to the thermometer, was made in two parts, the first part extending through and about one-half inch above the cork; the second part being the remainder of the stirrer as first described. The two parts are easily joined, with ample security, by means of a small piece of small bore rubber tubing. The advantage of such an arrangement in connection with the cork hardly needs further discussion.

The dark color gradually acquired by the bath from contamination with organic compounds can be readily cleared from time to time by adding a pinch of potassium nitrate and in this way continuous use for a large number of determinations is possible. I have myself made considerably more than 100 determinations without renewing the bath.

This method has been applied to the suggested standardization of the melting points of about 37 of the more important pharmacopœial compounds, involving from 4 to 8 or more determinations on each of 5 to 8 samples of the individual compounds (with a few exceptions). In making these determinations the bath was heated

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<sup>1</sup> S. P. Mulliken: "Identification of Pure Organic Compounds," vol. i, p. 219.

by direct application of a small Bunsen flame to the walls of the container, special care being taken in all cases to insure a definite uniform rise in temperature within a certain range of the melting point. Further details of manipulation will be briefly indicated in my discussion of the remaining causes of divergence.

The 37 compounds mentioned above are, with some exceptions, included only in that class of pharmacopœial compounds whose melting point determination by a capillary tube method offers no complication. I believe, however, that the application of this method to all other classes (such as fats, waxes, etc.) involves only modification in details and procedure and not any material change of apparatus. Furthermore, I can see no objection to applying it as a modification of Landolt's method in those cases where it would seem feasible and desirable to determine the melting point or freezing point of a compound by using a comparatively large amount, with the thermometer dipping directly into the substance.

As an official method doubtless some will criticize the one suggested as being too crude to insure the degree of accuracy and refinement that is desired in a standard value. But it seems to me that the principal object in the standardization of melting points—at least from the present view of the Pharmacopœia—is, not so much to adopt a method which will insure the *utmost* degree of accuracy and refinement attainable, however desirable that might be, as it is to adopt a method which shall be readily available to, and easily applied by, all concerned with the melting points of pharmacopœial compounds, and which shall be capable of reasonably concordant results as obtained by different manipulators, which after all is a very fair test of accuracy.

Though intending to be brief I have doubtless devoted more time to my discussion of methods than would perhaps seem desirable in the scope of a short paper involving other phases, but in any standardization the question of methods is the fundamental and probably the most important consideration—which fact may offer some justification for my slight elaboration upon this point. My indulgence, however, will necessitate a very brief discussion of the remaining causes if this paper is not to unreasonably encroach upon the other features of your programme.

That varying manipulation in melting point work may result in different values for the same compound has been experimentally demonstrated, and is further indicated by the recommendations of

the manufacturers' committee to the Committee on Revision of the U.S.P.

The so-called "personal factor" or "personal equation" (or other synonymous phrase) is doubtless a material and legitimate cause of divergence to some slight extent in any equally conscientious work; but it is also readily adapted to the service of a screen or shield covering careless, indifferent, and hurried manipulation. The amount of divergence honestly due to the "personal factor," I am strongly inclined to believe, would, in this instance, at least come well within the limits of a reasonably rigid standard, and for practical purposes may therefore be disregarded.

In so far as divergence is due to manipulation of the apparatus we believe it to be due largely, if not entirely, to differences in rate of heating and the variable application of stirring—entirely omitted in most cases; very irregular in others.

In describing the official method I would recommend, as a remedy for such defects, that the rate of heating for different stages of the determination be definitely prescribed and that constant stirring be required throughout the experiment.

Under differences in physical condition, as a cause of divergent values, there are three main considerations: (1) the size of the individual particles of the compound; (2) the moisture content; and (3) the presence of impurity.

Pawloff<sup>2</sup> has shown experimentally, working mainly with salol, that the more finely divided a solid is the lower is the melting point—the magnitude of difference depending in some measure upon the purity. He finds that a powder composed of particles less than  $2\mu$  (in diameter) melts, in the case of salol,  $7^{\circ}$ , in the case of antipyrine,  $5-7^{\circ}$ , and in the case of phenacetin,  $4^{\circ}$ , lower than particles of 0.5–2 mm. diameter.

Considering the wide range in size of the particles of the same product, as found in the market under different labels, the experimental results of Pawloff make it obvious that in order to eliminate this cause of divergence it is necessary to officially prescribe that all substances shall be finely powdered before being subjected to the melting point test.

The work of Tyrer and Levy, previously referred to in this paper, offers conclusive evidence, if any were needed, of the marked

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<sup>2</sup> *Zeit. Physikal. Chem.*, **65**, 1–35 (1908).

effect that the presence of moisture—also, of course, impurity—may produce upon the melting point of a compound. For example, in this connection, their results with acetanilide, phenacetin, and antipyrine show a variation in melting point of about  $1^{\circ}$  between the commercial and commercial-dried forms and a variation of from  $0.6^{\circ}$ , in the case of phenacetin, to nearly  $3^{\circ}$ , in the case of antipyrine, between the dried and the purified forms. The question of moisture as a cause of variation in the melting points of pharmaceutical compounds would seem to be easily disposed of by requiring a definite period of adequate desiccation for the finely powdered substances before the melting point determination is made.

The question of impurity, however, it seems to me, is a much more difficult one. To attempt an exact standardization of melting points for a class of compounds in which a certain percentage of impurity is permissible opens a wide field of investigation, that so far as I can find, has barely been touched upon, and constitutes, at least in theory, a very complicated problem, the discussion of which is far beyond the scope of this paper. Any possible difficulty in dealing with this factor, however, does not, in my opinion, justify neglect and tolerance of other causes of divergence which can be readily eliminated.

Passing rapidly over the topics remaining for discussion:

The fact that the use of thermometers of different construction induces more or less variation in results suggests the desirability of adopting an official thermometer—or set of thermometers—as a part of the official method, and requiring that they be standardized. True, such a step introduces the objectionable element of expense, but surely not in a prohibitive degree, even for a very modestly equipped laboratory.

That the application or omission of emergent-stem correction is a real and serious cause of divergence is strikingly illustrated by the fact that if a thermometer of average construction—used in connection with the apparatus we have recommended—registers  $200^{\circ}$  as the melting point of a compound, the correction, in most cases, will amount to  $3^{\circ}$  or  $4^{\circ}$ . Obviously uniformity of practice in this respect should be required, and in the cause of accuracy the correction should be applied. The manner of making the correction may also cause variation and should therefore be clearly defined—or better still, if official thermometers were adopted, official corrections could be made, plotted in a curve on co-ordinate paper and published,



and from this official curve the correction, for any temperature, could be determined by inspection, thereby conducing to absolute uniformity in this particular.

Finally, what is the melting point? Some authorities say it is that temperature at which the substance first begins to melt; others, that temperature at which it is just completely melted; others, the mean of these values; and still others say that it is not a point at all (except in theory) but a *range*, with which I emphatically agree.

At any rate it should need no argument to convince that here is broad opportunity for wide divergence; nor to induce the conclusion that if standardization of this constant is to be effective a clear, unmistakable definition of the melting point is essential.

With regard to the decomposing point I am personally convinced that it should never be used as a test of purity, and this conviction is based upon experimental evidence with several compounds.

Anything like a complete treatment of the melting point problem, in its present application to the U.S.P., is impossible within the limits of a half-hour discussion. For the purpose of this meeting it seemed more desirable to briefly outline *all* the more important phases of the problem than to attempt a very detailed discussion of any *one* or *two*.

Note: The subject of this paper, and the work that has recently been done in the Hygienic Laboratory on U.S.P. melting points will be given more complete and detailed treatment in a Hygienic Laboratory Bulletin to be published in the near future.

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#### CORRESPONDENCE ON THE RELATIVE VALUE OF MACERATION AND PERCOLATION.

In view of the statements contained in the Presidential address presented by Professor Oldberg to the members of the American Pharmaceutical Association at the Los Angeles meeting, on the subject of maceration, letters were sent to various persons, including both retail and manufacturing pharmacists, asking for their opinion on the relative merits of maceration and percolation. Abstracts of the replies received follow.—EDITOR.

Prof. H. V. Army, Cleveland, writes: I beg to make the fol-

lowing suggestions which have come from my personal experience.

I. Too little attention is paid in the average percolation to *loss of menstruum*, both by evaporation and through absorption of the marc.

II. Loss by evaporation can be prevented by suitable apparatus similar to that used ordinarily in percolation of volatile liquids (see "Economic Percolation," Proc. A. Ph. A., 1892, p. 169).

III. To make percolation profitable, the alcohol in the moist marc should be recovered. As to the two methods, that of percolating the marc with water and collecting the percolate approximating the amount of menstruum with which the marc was wet has never appealed to me. Far better is distilling the marc with steam, nor is this process one which should frighten the retailer. In my own retail experience I used a steam distilling apparatus consisting of a *boiler* made from a one-gallon tin can, provided with a cork with two holes, through one of which passed a straight safety tube, through the other a bent tube to convey the steam, which passed into the *distilling jar* which consisted of a wide-mouthed half gallon candy jar. I kept a half dozen such candy jars on hand for this purpose and the moist marc from every percolation (even though only an ounce) was transferred to the jar, which of course was kept tightly corked. The jars were only half filled with marc and when the six jars were thus half filled, the distilling apparatus was rigged up and the alcohol from the 10-12 pounds of marc was easily condensed, the jar being removed from the current of steam when the distillate was no longer alcoholic and replaced by another one containing undistilled marc. Since teaching, I have found it difficult to secure corks suitable for the candy jars, and have had made at the local can factory 1-gallon tin cans with larger mouths than ordinary—as large as will fit the largest corks now obtainable. These are in some respects not as satisfactory as the jars which in our drug business were so abundant that the occasional breaking of one meant no real loss. Of course the steam distilling apparatus must include a *condenser*, a fact so self-evident that I mention it merely for the sake of completeness.

IV. There is a lack of appreciation of the very great importance of careful percolation. Given the same drug and the same menstruum despite careful warnings as to speed of percolation, twenty operators will obtain as "first percolates" fluids of almost

twenty different strengths. I am now compiling figures showing amount of extraction in fluidextract of gentian made by repercolation from the same drug and the discrepancy in results obtained so far is extremely disappointing to one who has always been a staunch advocate of repercolation. Perhaps, however, my later figures will prove more satisfactory, but at present I can only advise utmost care in packing of drug and speed of percolation, and further recommend to all making their fluidextracts by repercolation, to compare the amount of extract in, say, 10 c.c. of the finished product with the amount of extract obtained with same menstruum on completely exhausting 10 grammes of the same batch of drug.

C. F. Nixon, Ph.G., Leominster, Mass., writes: I am afraid that I am strongly biased in this matter, so much so that I can conceive of no argument in favor of maceration where percolation is possible. The objections to maceration as they occur to me are as follows:

1. The drug cannot be properly exhausted unless several fractional macerations are employed and this requires much time.

2. Drugs prepared for maceration cannot be so finely ground as for percolation, as it would be impossible to express the saturated liquid. For example, tincture of belladonna, No. 60 powder, could not possibly be made by maceration.

3. Maceration must be accompanied by expression, and the amount of pressure used has a direct influence on the finished product. It would be impossible, however, to direct the amount of pressure used for each drug, and the results could not be uniform.

4. Unless much pressure is used there is a greater loss of menstruum.

5. It appears to me an uncleanly and unscientific process.

6. The product must be filtered. In many instances this would be a slow and difficult proceeding, as fine particles pass through in the process of expression that would clog the filter.

I believe that the adoption of maceration would be a long step backward.

May I add that the last official process for making tincture of arnica is most unsatisfactory, so much so that I think it is seldom employed. It seems to me that arnica is the very last drug that should be manipulated by maceration.

Prof. E. A. Ruddiman, Nashville, Tenn., writes as follows: My experience on "The Relative Value of Percolation and Maceration" has been limited, so far as comparing these two processes on individual drugs is concerned. I have found the pharmacopœial directions, as when to percolate and when to macerate, generally satisfactory. I cannot agree with Professor Oldberg in the statement made at the Los Angeles meeting of the American Pharmaceutical Association "that any plant tincture of 10 per cent. strength can be far more conveniently prepared by maceration than by percolation, and just as effectively." That has not been my experience either in the manufacturing laboratory or in the college laboratory.

Two preparations made by percolation that have given me trouble are fluidextract of squill and tincture of opium. In the case of the former I have had frequently to resort to maceration and straining, and clearing by standing. In the case of laudanum I am fully convinced from experiments which I have made in preparing this tincture and assaying the product, and in assaying the tinctures made by a large number of druggists, that the official process does not exhaust the drug. The opium should be exhausted as directed under the tincture of deodorized opium and the percolate evaporated if necessary.

In some cases I have found it desirable to use a coarser powder for percolation than directed by the Pharmacopœia.

E. L. Patch, Stoneham, Mass., says: While maceration may be advisable for gum-resinous drugs, or drugs largely soluble, as guaiac, myrrh, aloes, etc., for the larger number of ordinary drugs percolation is to be preferred.

If maceration is resorted to in such cases (ordinary drugs) and stirring of the drug and menstruum is followed, quite a portion of soluble matter is retained by the drug and can only be removed by strong pressure, which is usually inconvenient and annoying. If, on the other hand, the vessel has an outlet permitting the saturated or supersaturated liquid to flow off at intervals, as in percolation, more thorough extraction should result. We should remember that percolation is a process of solution and subject to the same rules as ordinary solution, and is affected by extent of surface exposed to action of solvent, to character of solvent, temperature, etc. The solvent may extract certain principles from the upper layers of drug in a percolator and become a compound



solvent, exerting a greater range of solvent action on subsequent portions. It is not necessary for percolation to be continuous. After two or three days' maceration, percolation can proceed until the percolate shows evidence of less saturation and then be stopped for another short period of maceration. We have noticed that a percolation conducted at a temperature of 50° compared with the same drug and menstruum at 70° requires more maceration and much slower percolation to obtain the same degree of extraction. While the fact is well known, the principle is often lost sight of. We recall being shown over the laboratory of a retail pharmacy where the percolations were being conducted near a large window in the coldest portion of the room because so much less time was required of the workers at the inconveniently low temperature than was required at other processes. At the time of our visit the temperature was about 45° F. and the operator was not properly extracting his drugs. For general use the instructions of the Pharmacopœia, as to method of conducting percolation, are sufficiently explicit.

Wilbur L. Scoville, Detroit, comments as follows on this subject: I have never done any direct work on the comparative results of preparations made by maceration with those made by percolation. I am aware that the maceration process produces a tincture that is less prone to precipitate but under the best of conditions it is more wasteful, and the precipitation in the percolation process can be reduced to a minimum by mixing all the menstruum necessary before beginning, and so avoiding slight changes in the menstruum during the process. Furthermore, except in the cases of a very few oleoresinous, resinous, and astringent drugs, the active principles of which are easily accessible and quickly soluble, maceration is the more important part of percolation. Pressure percolators have been proved inadequate many times, and long macerations, seven to ten days, are frequently an advantage, particularly in making concentrated preparations.

While a trained worker, taking special pains in a series of comparative experiments, may show some superior results for the maceration process, I believe that the average worker, on whom the necessity for full maceration and slow percolation has been impressed, will get more uniform, and on the average better, results by the process of percolation. This is, however, a tribute to maceration quite as much as to percolation.

Prof. Philip Asher, New Orleans, contributes the following: An experience of twenty-two years in pharmaceutical laboratories with both methods is decidedly in favor of percolation.

In the case of the exudates, as asafetida, myrrh, etc., it has proven more satisfactory than maceration and obviates the unnecessary cleansing of the utensils, so common with the latter process.

The following has been the *modus operandi* employed: The receptacle is graduated. The neck of the percolator is plugged with cotton moistened with alcohol. Over this a layer of well-packed excelsior is placed, acting as a porous diaphragm. The asafetida is placed in the percolator and some alcohol added, but not sufficient to cover the asafetida. This is allowed to macerate a short time, after which the asafetida is disintegrated by *poking* it with a sharp stick. After standing a short while to allow settling, percolation is started, and the disintegration repeated if necessary. Instead of adding the required menstruum at once, it is preferable to add only sufficient to leave a small layer above the drug.

The above process followed as outlined exhausts the asafetida completely, long before all the menstruum has been used, as evidenced by lack of precipitation when a few drops of the percolate are permitted to fall into water.

By this method, the so-called fluid asafetida, as offered by the pharmaceutical houses, can be made, heat being absolutely unnecessary in any of the stages, which represents 50 per cent. of the soluble principles.

Dr. J. M. Francis, Detroit, discusses the subject as follows: Without entering into any prolonged discussion of the matter, we beg to say that our experience would seem to indicate that maceration in the original sense is not at all necessary and is not nearly so satisfactory, all things considered, as percolation when properly conducted. Consequently we believe we are correct in saying that the old form of maceration is hardly ever employed in our laboratory at the present time.

It might be well for the sake of clearness to state that by "maceration" we refer to the old procedure whereby an excess amount of liquid is placed in contact with the drug and allowed to stand or macerate for several days, the liquid then being decanted or drawn off; a fresh portion of liquid in excess being added to the drug, maceration continued, and the process repeated.

Of course the ordinary process of percolation always involves a certain amount of maceration. The Pharmacopœia directs that a drug shall be moistened, allowed to swell through the absorption of the liquid, then be transferred and properly packed in a percolator, be covered with menstruum and allowed to macerate or "soak" for a certain length of time; and the percolation is then carried out in the usual way. Such maceration as this, where only a relatively small amount of liquid is employed, is very necessary. Even where the menstruum is allowed to slowly flow upon the drug in process of percolation, maceration is taking place unless the passage of the liquid through the drug is carried on with undue rapidity. Maceration, however, involving the use of an excess of liquid and long standing, we consider wholly unnecessary and we do not find it desirable even in the manufacture of tinctures.

The above statement is the outgrowth of long and continued experience. You may perhaps remember that in the beginning all of our fluids were prepared by this process of maceration. The drugs were allowed to stand in contact with the liquid for days, sometimes for weeks, the liquid was drained off, and the marc was then placed in a hydraulic press and the remaining portion of the liquid contents were pressed out. This old process, while yielding very good results, was found to be very expensive in time through the loss of menstruum, and moreover yielded fluids which showed a marked tendency to precipitation on standing.

Prof. Leo Eliel, South Bend, writes: There has been so much said and written on the relative value of percolation and maceration in pharmaceutical operations, that it would seem as though the last word had been said. This subject has been under discussion for fifty years to my knowledge. But the fact that you are taking up this subject for discussion at your pharmaceutical meeting would seem to show that there is still something to differ on.

As you are asking for my personal experience, I would say that it is decidedly in favor of the process by percolation; my reason for this being that by this process it is possible to have a definite quantity of the soluble drug constituents in a definite quantity of fluid. This is not the case in maceration, as there will always be an indefinite amount of soluble constituents left in the marc. However, I might say that the official directions, in many cases at least, do not allow a sufficient length of time for maceration before percolation. My practice is to macerate for a period of from three

to five days before packing and percolating. Of course with such drugs as zingiberis this would not be required, neither would this apply to mucilaginous drugs, where it might release substances that retard percolation.

H. A. B. Dunning, Baltimore, presents the following view of the subject: In most processes used for the extraction of vegetable drugs by means of solvents, maceration forms a necessary part, but whether the complete extraction of the drug should be accomplished through continued maceration is a doubtful question.

While it must be admitted that the active constituents of vegetable drugs may be entirely extracted by maceration, there are, I believe, very decided objections to this method, in practice. The *modus operandi* in my opinion is cumbersome, requiring, frequently, the introduction of comparatively large quantities of powdered material into narrow necked bottles, which material subsequent to exhaustion with the menstruum must be removed. Besides the stock bottle, a stock container and also a maceration vessel is required.

It is a tedious method, requiring seven days and oftentimes more for completion, depending largely on the attention given it.

It is apt to be uncleanly because, due to the frequent agitation necessary, some of the liquid may be allowed to escape from the container and run over it: of course the use of a little water would obviate this objection. Besides, when mixtures are poured from one vessel to another spilling is likely to result, not mentioning loss.

The process is also likely to be inaccurate, depending greatly upon the personality of the operator. for if the mixture is not frequently agitated, extraction will be very imperfect in the time usually designated; particularly is this statement true in regard to drugs which have a tendency to form "gummy" masses when moistened. In this case the final resort is "poking" with a stick: sometimes the stick is poked on through the bottle or other container. Further, I am told by some of the older pharmacists, who have had a more extensive experience with this process than I, that it is all too frequently the practice of some persons to use a portion of the macerating preparation before the time allowance is complied with and that in many instances no adjustment is subsequently made.

The maceration processes of the German, French, and English Pharmacopœias direct that the required amount of drug be macer-



ated with a definite volume—weight in case of German and French Pharmacopœias—of menstruum, the mixture strained, and marc expressed, the liquids then mixed and filtered. There is no allowance made for increase in volume through the dissolved extractive matter. The finished preparations are therefore neither of known percentage or part solutions. The U. S. Pharmacopœial method avoids this, perhaps slight, inaccuracy.

There are a few points in the various pharmacopœias, regarding maceration and percolation which seem inconsistent to me, although, I grant, that there may be good reasons, which do not appear on the surface. I do not understand why the British authority directs compound tincture of cinchona to be prepared by percolation and compound tincture of gentian by maceration; nor do I comprehend why the British Pharmacopœia as well as the German authority directs fluidextracts, which represent a much larger proportion of drug than do the tinctures, to be prepared by percolation, while some of the British and all of the German tinctures are prepared by maceration.

There are several tinctures directed to be prepared by maceration by the U. S. Pharmacopœia, which, although I have heard reasons given for so doing, in accordance with my experience would be better prepared by percolation.

I find the process of maceration entirely unsatisfactory for the preparation of tincture of arnica, inasmuch as the drug acts much like a sponge, absorbing by far the greater portion of the menstruum with which it is macerated, and it is a very difficult proposition to express much of the adhering liquid, even by means of a "press." Besides the filtered tincture is not so clear and rich in color as that prepared by percolation. I might mention that I have frequently observed that in passing menstruum through a drug the latter while being extracted acts as a clarifying agent. In regard to the best method for the preparation of this tincture and other tinctures presenting similar difficulties, I recommend for consideration the English method of collecting a large portion of the required volume as a reserve percolate and then expressing the marc. I make this suggestion only in case a dreg still is not at hand or the fluid cannot be forced from the marc by water (I have rarely found this latter suggestion expedient).

I have recently had under observation a series of experiments with different processes for the preparation of compound tincture

of cardamom. The conclusions drawn from these experiments are as follows: The present U.S.P. method is entirely unsatisfactory. Besides having the shortcomings of all maceration processes the product was filtered with great difficulty; and the filtrate was by no means as bright and clear as that made by percolation. I did not observe much difference in the quantity of deposit, on standing. The addition of glycerin to the menstruum previous to extraction only serves to increase the proportion of inert extractive. It should, I believe, be added after percolation.

In the preparation of tincture of opium the drug could be extracted more readily if it were mixed with some inert non-adhesive material, like purified sawdust or powdered paper. In this connection it might be well to mention that, in my experience, it is difficult to completely exhaust opium by the prescribed amount of menstruum and I would suggest that it might be well to percolate the drug to exhaustion with a suitable menstruum after having set aside a reserve portion; the weak percolate being evaporated to a soft extract and dissolved in the reserve percolate, etc.

Tincture of aloes and compound tincture of lavender now prepared by maceration are both suitable for the process of percolation.

Referring to percolation, I may state without hesitation that this method of extracting drugs appeals to me very forcibly. It should be preceded, as is invariably directed by the leading authorities, by sufficient maceration to soften and disintegrate the cellular tissue, within which the extractive matter is enclosed. Indeed maceration to this extent is a part of the process of percolation. This process, in my opinion, avoids almost entirely the objections offered to the *modus operandi* of maceration. Even the temptation to abstract portions of the unfinished product is obviated because of the comparatively less length of time required for completion of the process when once in active operation. Yet it is true that the time of maceration, before percolation, may be cut.

The entire theory of percolation is convincing and I believe the theory is well borne out in practice. I know of no serious objection to this process unless, as I have sometimes heard stated, the final product after standing shows a greater proportion of inert sediment than does a like preparation made by maceration. This may be true, due to the action of solutions of extractive matter of different degrees of saturation upon different portions of the drug and the subsequent mixing of same. However, I have ob-

served no very great difference in this respect between the products of the two processes under consideration.

I hold very strongly the opinion that all drugs that are suitable to be extracted by maceration or percolation should be treated by the process of percolation, provided that the material is not of such character that the particles, when moistened with the proper menstruum, will adhere so closely that the menstruum does not properly permeate the mass, or when the characteristics are such that it would be harmful to the substance to reduce it to a state of division suitable for percolation. The degree of fineness should be sufficient to avoid permitting the menstruum to pass freely through the spaces between the particles of the drug. Finally, it is my belief, that those pharmacists who have become familiar with the process of percolation will endeavor to avoid maceration processes.

Irwin A. Becker, Ph.G., Michael Reese Hospital, Chicago, writes that the only U.S.P. process for tinctures which he has modified is that for tincture of capsicum, his process being as follows: The drug is macerated for from three to five days, followed by filtration, the marc being transferred to the filter as early in the process as practicable. Sufficient menstruum is added through the filter to give the required measure. The resulting tincture usually has a deeper color and appears more brilliant than that made by percolation. Tinctures were made from four different purchases of drug, three being those from local jobbers and the other being Gilpin, Langdon & Company's "powdered capsicum for percolation." One of the observations in this series of experiments was that while G. & L.'s powder was lighter in color than the others, the tincture is as deep colored as those made from the other powders.

Mr. Becker incidentally mentions that he has trouble in removing the last traces of petroleum benzin in the process for tincture of deodorized opium.

## AMERICAN PHARMACEUTICAL ASSOCIATION.

## SECTION ON PRACTICAL PHARMACY.

Our annual meeting will soon be here and the Committee on Practical Pharmacy and Dispensing, *the* section for the practical retail pharmacist, is soliciting papers.

Being a Pharmacopœial Convention year, constructive papers on U.S.P. subjects will be greatly appreciated and will also be helpful to the U.S.P. Revision Committee as well as to the members in general.

Select your subject as soon as possible, and in order to avoid duplication send in the title of your paper *now*.

Give this matter your immediate attention and let us make the Richmond meeting the most important, the most interesting, the most instructive, and the most enthusiastic in the history of the A. Ph. A.

OTTO RAUBENHEIMER,  
Chairman.

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PHILADELPHIA COLLEGE OF PHARMACY.

## FEBRUARY PHARMACEUTICAL MEETING.

The stated pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday, February 15, at 3 o'clock, with E. M. Boring in the chair.

Dr. D. W. Horn read a paper entitled "Is there Caramelization in Rivas's Test?" (See p. 151.)

The paper was a suggestive one, and those taking part in its discussion were Dr. C. S. Brinton, Professors Remington and LaWall, and Messrs. R. W. Hilts, W. L. Cliffe, and the chairman. Professor Remington said there were some who claimed that the color of straight whisky stored for four years in charred barrels is due to caramel produced by the action of heat on the wood in the charring process, and asked in what respect the color of straight whisky differs from that of true caramel, at the same time stating that there are those who claim that the caramel-colored whisky is just as good as straight whisky. He then remarked that a reliable test would have to be found for whisky.

As instances of the darkening of sugary preparations, Mr. Boring cited that of commercial syrup of hydriodic acid when partly used,



and Professor LaWall that of Eastman's syrup, which contains strong phosphoric acid.

Dr. Brinton called attention to the fact that glucose is not a chemical compound, but is a mixture including dextrin and other foreign substances. He also spoke favorably of Marsh's test for caramel.

Prof. LaWall asked if Dr. Horn had performed any experiments to determine the specific action of different strong acids on sugar solution since he had assumed that in the syrup of ferrous iodide the sugar was hydrolyzed or "inverted" by the free hydriodic acid. Prof. LaWall also asked if Dr. Horn had tried to extract the "aldehyde resins" with immiscible solvents.

In answering the several speakers, Dr. Horn said: In his experiments he had used the well-defined chemical compound, the crystallized mono-hydrated d-glucose, and not the commercial syrupy mixture that Dr. Brinton evidently had in mind. Marsh's test, although it might well be satisfactory in testing *acid* liquids like whisky, was unreliable in testing *alkaline* liquids. With regard to a statement of Dr. Brinton's that alcohol after treatment with alkali may acquire a yellow color and yet not answer the test for aldehydes, Dr. Horn said that small quantities of aldehydes might readily be formed by the action of atmospheric oxygen on the  $\text{—CH}_2\text{OH}$  group of the alcohol. Replying to Prof. LaWall, Dr. Horn said that he had not been interested in the specific action of different acids, and that this had no bearing upon his paper, for he had referred to the action of hydriodic acid at such dilutions that the action was to be ascribed to the hydrogen ion, and that at such dilutions all acids of the same class as to strength would yield hydrogen ions at approximately the same concentration. The anion produced no appreciable effect at these dilutions. He said that he had not tried the action of immiscible solvents, and that he was not convinced that the so-called "aldehyde resins" of the organic chemist were the same in character as the resins Prof. LaWall had in mind. Referring to the brown color of whisky mentioned by Professor Remington, Dr. Horn said that in the recent literature there was a paper showing that the brown sediments sometimes appearing in whiskies were aldehyde-compounds. Regarding the odorous principle that he separated from the brown solution, he stated that he had not yet had time to study it further, but that the solutions containing it sustained the life of some molds and that in so doing they lost their odor. In this connection, he

pointed out that caramel purified by dialysis is not described as having an odor.

Dr. Brinton called attention to an observation that in separating aldehydes from alcohol by treating with alkalies the color disappears even on standing, and that aldehydes do not appear to be present except in alcohol from colored barrels. Dr. Horn remarked that sufficient of the oxygen of the air would gain access under the conditions to produce aldehyde, and stated that sealing in glass was necessary to prevent the access of air.

Professor LaWall referred to the popular notion that the burning of sugar has a disinfecting action and to the claim that formaldehyde is one of the resulting products. Mr. R. W. Hilts stated that a French chemist had found that smoked meats and sausages will give the reaction for formaldehyde, and that in the burning of a number of carbonaceous (carbohydrate) substances, formaldehyde is produced.

George M. Beringer, Ph.M., presented some notes on the U. S. Pharmacopœia, stating that he desired to direct attention to one specific subject—namely, the relation of the practical pharmacist to the work of revision. He called attention to the minutes and reports of various committees on the U.S.P. of the Philadelphia College of Pharmacy going back to the earlier revisions, and in commenting on the amount and importance of their work said that he made the exhibit to show that retail pharmacists always took part in the work. The speaker contended that if retail pharmacists do not take up the various practical problems, then it is their fault if the Pharmacopœia is found better adapted to the needs of manufacturers and others. He said that every pharmaceutical society and every college of pharmacy should take part in the work with a view of making the Pharmacopœia the legal standard for those who follow it and who must stand by it.

Mr. Beringer said that no matter what physicians say in regard to admissions and deletions, the pharmacist must stand his own, the trouble with many physicians being that they are working on questions that especially interest them. As an illustration of this tendency he said that recently one of them had suggested the omission of *krameria* and its preparations, while according to his own experience they should be retained.

With regard to the dosage forms of medicines, he said it was clearly within the province of pharmacists to work out the formulæ for them, as for example in the case of phenolphthalein. As

examples of official preparations requiring an improvement in the formulæ and directions, compound tincture of gentian and fluid-extract of squill were mentioned. Continuing, Mr. Beringer said that Dr. Rusby's paper on "Crude and Powdered Drugs at the Port of New York during the Year 1907-08" (*AM. JOUR. PH.*, 81, p. 231; *Proceedings A. Ph. A.*, 1908, p. 783) shows the extent to which certain foreign drugs are being imported and used in this country, and of these he mentioned mylabris (Chinese beetle), stating that according to his experiments this drug is not adapted for the liquid preparations owing to the excessive amount of fat present, but that it is suitable for the plaster, and that if admitted to the Pharmacopœia retail druggists should have the say as to which preparations it should enter. Saw palmetto was mentioned as an example of an official drug for which no formula was given, and the claim made that pharmacists should work out formulæ for preparations of it.

Professor Remington said with reference to Mr. Beringer's remarks that the physician could not be blamed for looking at these questions from his point of view, nor druggists from theirs, nor even chemists from theirs, one of them, B. L. Murray, having recently proposed the omission of iron and mercury from the Pharmacopœia. With regard to mylabris and many other imported drugs, he stated that the desire to make them official was based on the need of standards for them.

John K. Thum, Ph.G., presented some notes on the Pharmacopœia, and offered the following practical suggestions based in part on his own experience: (1) That benzoinated lard be prepared by dissolving 1 per cent. of benzoic acid in lard melted at a low heat; (2) that in view of the statements that the stronger the alcoholic menstruum the more stable the preparations of digitalis coupled with the opinion that deterioration of these preparations is due to a ferment, experiments should be carried out along the line of extraction with a stronger menstruum and in the making of quantities, as of the tincture, which would be used in a short time; (3) that antiseptic solution should not be retained in the Pharmacopœia and that the addition of glycerin would make it more palatable, while maceration with 0.40 Gm. of finely ground golden seal for 24 hours followed by filtration without the use of talcum would improve its appearance; (4) that the addition of 10 per cent. of glycerin to the formula for compound syrup of hypophosphites enhances both the appearance and keeping quality, and that an

increase of the sugar from 775 Gm. to 825 Gm. per liter causes neither precipitation nor fermentation; (5) that in the definition of ether the words "not less than 96 per cent., by weight of absolute ether or ethyl oxide" should be substituted for the words "about 96 per cent., etc.," and that the time limit of the test for aldehyde should be extended; (6) that the description of each crude drug should be followed by a list of all the official preparations into which it enters; (7) that whenever an official compound is made and sold by different manufacturers under different names, as hexamethylenamine, the Pharmacopœia should state that these apply to compounds similar to the official one; (8) that the ten official syrups now directed to be made by the use of fluidextracts should be made direct from the drug, for the reason that when made from fluidextracts from which the precipitates formed by aging have been removed, they do not represent the full medicinal value of the drug.

Dr. C. S. Brinton, chemist of the U. S. Food and Drug Inspection Laboratory, Philadelphia, read a paper on "The Pharmacopœia in Food and Drug Inspection Work," which may appear in a later number of this JOURNAL, and in connection with the presentation of which a number of interesting specimens were exhibited.

Referring to the subject of powdered asafetida, Mr. Boring said that physicians have very little idea of the physical character of the drug and that when it is ordered on a prescription he selects the tears, which are free from impurities, and powders them, and that furthermore the gum having the character of an emulsion, it is not difficult to effect its solution when ordered in this form.

Dr. Horn, in alluding to the subject of revision, said that there is one good book on organic chemistry—namely, Beilstein's Organic Chemistry; that it had been gotten out well once, and that it is being revised all the time, small volumes being added from time to time. Professor Kraemer called attention to the manner of revision of the Japanese Pharmacopœia, stating that while the new Pharmacopœia was being considered, certain subjects were published as addenda to the previous edition, thus permitting opportunity for criticism and revision.

On motion of Professor Kraemer a unanimous vote of thanks was tendered the speakers of the afternoon for their interesting and valuable papers.

FLORENCE YAPLE,  
Secretary *pro tem.*



# THE AMERICAN JOURNAL OF PHARMACY

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MAY, 1910

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## A NOTE ON A SUITABLE ULTIMATE STANDARD FOR THE VOLUMETRIC SOLUTIONS OF THE U. S. PHARMACOPŒIA.

BY ELIAS ELVOE.

The very prominent position given to volumetric analysis in the U. S. Pharmacopœia, and its almost exclusive use, wherever possible, in determining whether a given substance comes up to the required standard of purity, render it imperative that the most suitable ultimate standard be adopted for the necessary volumetric solutions. It is also obvious that in considering what substance might form a suitable ultimate standard for these solutions, we must place as of primary importance the readiness with which such substance is obtainable in a pure state, its stability under ordinary conditions, its possessing the necessary properties for admitting of its use in a volumetric process of proven accuracy, and, finally, what likelihood there is of different operators obtaining such substance in different degrees of purity although working by the same method.

The substance chiefly relied on as standard in the present U.S.P., namely, potassium bitartrate, although meeting these requirements quite satisfactorily in many ways, nevertheless appears to present the disadvantage of introducing a personal error in the procedure for its purification. Thus Parsons,<sup>1</sup> who investigated the suitability of this substance as a means for the standardization of acid and alkaline solutions, states that he "made up some according to the directions given . . . but found it necessary, in order to get the pure salt, to crystallize three times in addition." He also

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<sup>1</sup> *Jour. Anal. Chem.*, 6, 380-381 (1892).

states that this salt has a "tendency to retain an excess of acid, probably tartaric, set free in small quantity by the hot hydrochloric acid."

The more or less undecided state of this question of the most suitable substance for use in standardizing volumetric solutions may also be seen from the very large number of substances which have been proposed for such use by different authors.<sup>2</sup> Thus for standardizing acids and alkalies, Reinitzer (*Zeit. anal. Chem.*, **34**, 575) uses sodium carbonate; Grandeau (*Ibid.*, **2**, 426) and also Pincus (*Ibid.*, **2**, 426) use Iceland spar; Sørensen (*Ibid.*, **40**, 115) uses sodium oxalate; Rimbach (*Ibid.*, **32**, 449) uses borax; Hartley (*Ibid.*, **12**, 89) uses metallic sodium; Seyda (*Ibid.*, **39**, 458) and also Weinig (*Ibid.*, **32**, 450) use ammonium chloride; Knublauch (*Ibid.*, **21**, 165) uses ammonium sulphate; Fessel (*Ibid.*, **38**, 449) uses potassium iodate; Reichardt (*Ibid.*, **13**, 49) uses oxalic acid; Ulbricht and Meissl (*Ibid.*, **26**, 350) use potassium tetroxalate; Bornträger (*Ibid.*, **25**, 333) uses potassium bitartrate; Richter (*Ibid.*, **21**, 205) uses potassium dichromate; Meineke (*Ibid.*, **35**, 338) uses potassium biniodate; Guyard (*Ibid.*, **24**, 585) uses boric acid; Petersen (*Ibid.*, **41**, 165) uses succinic acid; Riegler (*Ibid.*, **35**, 308; **38**, 250) uses iodic acid; while Hart and Croasdale (*Ibid.*, **31**, 190; **33**, 455) obtain a standard sulphuric acid solution by electrolyzing pure copper sulphate.

Similarly, for standardizing potassium permanganate, Riegler (*Ibid.*, **35**, 522) uses oxalic acid; Ulbricht and Meissl (*Ibid.*, **26**, 350) use potassium tetroxalate; Sørensen (*Ibid.*, **41**, 169) uses sodium oxalate; Gräger (*Ibid.*, **6**, 209) uses ferrous oxalate; Stolba (*Ibid.*, **18**, 600) uses lead oxalate; Schöne (*Ibid.*, **18**, 137) uses piano (iron) wire; Pawolleck (*Ibid.*, **41**, 172) uses ferrous ammonium sulphate; Biltz (*Ibid.*, **41**, 173) uses ferrous sodium sulphate; Gintl (*Ibid.*, **6**, 447) uses potassium ferrocyanide; Wdowiszewski (*Ibid.*, **41**, 174) uses iron oxide; while Erlenmeyer (*Ibid.*, **18**, 291) uses lead sulphocyanate. For standardizing iodine solutions, Kalmann (*Ibid.*, **26**, 728) uses sodium sulphite; Bobierre (*Ibid.*, **8**, 505) uses sodium arsenate; Zulkowsky (*Ibid.*, **41**, 184) uses potassium dichromate; Crismer (*Ibid.*, **25**, 553) uses normal potassium chro-

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<sup>2</sup> A very useful contribution to the literature on this subject, which has been freely made use of in this connection, is a paper by Vanino and Seitter in *Zeit. anal. Chem.*, **41**, 141-218 (1902).

mate; Riegler (*Ibid.*, 35, 305) uses iodic acid; Fessel (*Ibid.*, 41, 187) uses potassium iodate; Meineke (*Ibid.*, 35, 338) uses potassium biniodate; Kratschmer (*Ibid.*, 24, 546) uses sodium bromate; while Metzl (*Jour. Chem. Soc.*, 90, ii, 194) uses potassium antimonyl tartrate.

We may, perhaps, also gain an idea as to some of the reasons why apparently not a single one of the substances above mentioned has met with entire satisfaction generally, if we recall some of the remarks made by various authors concerning some of the substances in the above list which appear to have been used most. Thus, according to Morse,<sup>3</sup> the substance which has been longest and probably most frequently employed for the standardization of acids is the neutral anhydrous carbonate of sodium. The latter is also recommended by Sutton.<sup>4</sup> As is well known, however, this salt is hygroscopic and hence great care must be taken in handling it. Thus, according to Morse, the portion of the material which is to be used in any experiment should be reheated in a small platinum crucible or boat, cooled in a desiccator, and protected from the moisture of the air while weighing by inclosing it in a weighing glass. It has also the disadvantage that it is liable to appreciable decomposition if the temperature is not strictly regulated while it is being heated in order to convert all the bicarbonate into the normal salt. Thus, according to Seyda,<sup>5</sup> sodium carbonate is likely to retain excess of CO<sub>2</sub>, or if overheated it may contain sodium hydroxide. Similarly, in the case of potassium tetroxalate, which is recommended for standardizing purposes by Kühling<sup>6</sup> and also by Morse,<sup>7</sup> Lunge<sup>8</sup> states that he has never been able to prepare a potassium tetroxalate in which the water of crystallization corresponds accurately with the formula C<sub>2</sub>O<sub>4</sub>HK.C<sub>2</sub>O<sub>4</sub>H<sub>2</sub>.2H<sub>2</sub>O. In the case of oxalic acid, the disadvantages which may be mentioned, on the authority of Morse,<sup>9</sup> are that the commercial article contains acid oxalates from which it cannot be readily freed by the ordinary process of recrystallization from water and that it cannot be dried

<sup>3</sup> Morse: Exercises in Quantitative Chemistry (1905), p. 127.

<sup>4</sup> Sutton: Volumetric Analysis, 9th ed., p. 42.

<sup>5</sup> *Jour. Chem. Soc.*, 78, ii, 44 (1900).

<sup>6</sup> *Ibid.*, 86, ii, 80 (1904).

<sup>7</sup> Morse: Exercises in Quantitative Chemistry (1905), p. 126.

<sup>8</sup> *Jour. Chem. Soc.*, 86, ii, 771 (1904).

<sup>9</sup> Morse: Exercises in Quantitative Chemistry (1905), pp. 116-117.

in a desiccator, since in an atmosphere devoid of moisture it loses water of crystallization. Finally, Iceland spar, which has recently been advocated by Rose,<sup>10</sup> has the disadvantage that much of the material now sold under that name contains magnesium carbonate.<sup>11</sup>

On the other hand, of all the volumetric processes at present known, there is probably not one that excels in elegance<sup>12</sup> or accuracy the well-known Volhard method for titrating silver by means of a thiocyanate solution. In fact, its advantages are so pronounced that Shutt and Charlton<sup>13</sup> have even recommended its use in estimating the very small amounts of chlorine in potable waters, in preference to the standard chromate method; while the maximum error of Rosanoff and Hill,<sup>14</sup> when applying this method to the estimation of chlorides by precipitating with a known excess of silver and determining the remaining silver in the filtrate, was only 0.17 per cent. Finally, we need only mention the fact that Stas,<sup>15</sup> in his classical atomic weight work, did not estimate silver or chlorine gravimetrically but by titration by the method of Gay-Lussac. Likewise, Richards,<sup>16</sup> in his revision of Stas' work, estimated silver and chlorine by titration with the aid of his nephelometer. It is thus seen that the experience of chemists has been that, in the case of silver, the available volumetric methods may even exceed in accuracy the gravimetric process; while the high value of the latter, as a means for standardizing volumetric solutions, has been expressed by more than one author.<sup>17</sup> If, therefore, we should base the standardization of all, or at least most, of our

<sup>10</sup> *Chem. Eng.*, 10, 204-206 (1909).

<sup>11</sup> Morse: *Exercises in Quantitative Chemistry* (1905), p. 125.

<sup>12</sup> Vanino and Seitter express themselves in such connection as follows: "Hierher zählen bekanntlich die elegantesten und genauesten Methoden der Maassanalyse, wie wir solche in denjenigen von Gay-Lussac, Mohr, Volhard, und Liebig besitzen und welchen sammtlich eine—Silbernitratlösung—zu Grunde liegt."—*Zeit. anal. Chem.*, 41, 194, (1902).

<sup>13</sup> *Jour. Chem. Soc.*, 90, ii, 894 (1906).

<sup>14</sup> *Jour. Amer. Chem. Soc.*, 29, 273 (1907).

<sup>15</sup> Richards: *Ibid.*, 27, 461 (1905).

<sup>16</sup> *Jour. Amer. Chem. Soc.*, 27, 502-510 (1905).

<sup>17</sup> Parsons: "I have no hesitancy, when convenience is also taken into consideration, in placing the determination as silver chloride at the head of gravimetric methods," for standardization purposes.—*Jour. Anal. Chem.*, 6, 373-374 (1892). Phelps and Hubbard: "The previously most valued standard—hydrochloric acid standardized gravimetrically as silver chloride."—*Amer. Jour. Sci.*, 23, iv, 213 (1907).



volumetric solutions on this method, we would obtain not only convenience and general ease of manipulation but also a very high degree of accuracy.

As to the comparatively great ease of obtaining pure metallic silver we need only mention the following facts. In his revision of Stas' atomic weight for chlorine, one of the samples of silver which Richards<sup>18</sup> used was sent to him from the Colorado Smelting Works at Argo, Colorado. This specimen was stated to be the product of the treatment of ores in which it occurs associated with quartz, barite, calcite, pyrite, sphalerite, with more or less copper in the form of chalcopyrite, together with small amounts of arsenic, antimony, lead, bismuth, and tellurium. To recover the silver, the ore is roasted, mixed with other ores which are chiefly siliceous, and the mixture is so arranged that when smelted it yields a slag, containing about 40 per cent. of silica, and a first matte of fusible sulphide, which assays about 40 per cent. of copper, 10 per cent. of lead, and 400 ounces of silver and 6 ounces of gold per ton. The next stage in the process includes the roasting and concentration of the ore-metal, or first matte, to "white metal" containing about 60 per cent. of copper. The silver is then extracted from this white metal by the following operations: Rough roasting, fine grinding, fine roasting for sulphate of silver by Ziervogel's process, leaching and the precipitation of the silver on plates of copper. In the precipitation of the silver a certain amount of copper is found mixed with the silver in the form of cuprous oxide and of small scales and scraps of metallic copper. This copper is removed by prolonged boiling with water containing a small quantity of sulphuric acid, into which air is injected by means of a small jet of steam. Sulphate of copper is thus formed, which is carefully washed out of the silver. The silver is then dried and melted into bars of an average fineness of 99.9 per cent. The specimen of silver actually obtained by Richards, however, the latter found to be even purer than is indicated by the above figures. We thus see that although starting with a very complex natural mixture, containing many different elements, only a very small fraction of which is the desired silver, this metal is actually obtained on a large commercial scale of a degree of purity almost approaching absolute purity. Can this be said of any of the other numerous substances which have been proposed as standards in volumetric analysis?

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<sup>18</sup> *Jour. Amer. Chem. Soc.*, 27, pp. 474-475 (1905).

But even if it should be desired to obtain the metallic silver in a condition which may be regarded as absolutely pure for all analytical purposes, it can readily be obtained by electrolyzing a solution of silver nitrate, as shown by the work of Gooch and Perkins;<sup>19</sup> while if it also be desired to use precautions taken by Richards in his atomic weight determinations, we need only fuse the silver in a boat of pure lime placed in an atmosphere of hydrogen. In other words, if we adopt pure metallic silver as the standard for our volumetric solutions, we enable chemists and pharmacists to obtain such standard, even commercially,<sup>20</sup> in a condition not requiring further purification, or to prepare same in the laboratory with comparatively very little work. It would probably also avoid such dissimilarity of results as that seen in the case of potassium bitartrate, for example, which, as already mentioned, Parsons states that although following Bornträger's directions, he had to recrystallize three times in addition in order to prepare the pure salt; or the different results obtained by Lunge when studying Kühling's potassium tetroxalate, to which reference has already been made.

And we can also readily see why there should be such a striking difference between metallic silver as the standard and most of the other substances which have been proposed for this same purpose. For in the case of metallic silver we are dealing with an element—a substance which is undecomposable by any means at present known—whereas in the case of most of the other substances proposed as standards, we are dealing with compounds, many of which are more or less easily hydrated, some of which are hygroscopic, and nearly all of which are more or less soluble in water and hence readily affected by moisture.

The advantages of metallic silver as the ultimate standard in volumetric analysis are, however, not entirely due to its elementary nature but largely to its own peculiar properties. Thus, when com-

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<sup>19</sup> *Zeit. anorg. Chem.*, **63**, pp. 322-323 (1909).

<sup>20</sup> It is interesting to note in this connection the various descriptions given to Merck's "Tested Reagents." Thus we note: Potassium tetroxalate, for use in "preparation of volumetric solutions." Sodium carbonate, anhydrous—for use as "starting material for preparation of volumetric solutions." Oxalic acid—for use in "preparation of volumetric solutions." Potassium bitartrate—for use as "starting material for preparation of volumetric solutions." Silver sheets, for use in "standardizing volumetric solutions." (Prices and Uses of Tested Reagents, Merck & Co., New York, 1909).

pared with such an element as iron for example (which is quite often used in standardizing  $\text{KMnO}_4$  solutions), silver offers the additional advantages of being much more readily prepared in perfectly pure state, in being suitable for a volumetric process in which atmospheric oxidation can have no influence, and in being suitable for long keeping unaltered. To illustrate the last mentioned property of silver we need only recall that when at the request of Dumas, Stas<sup>21</sup> repeated (1890) his work on silver, he found that the silver which he used in his atomic weight determinations (probably about 1860) contained an altogether insignificant amount of gases, in no case greater than the unavoidable experimental error. In other words, although many years had elapsed between the two investigations, yet Stas apparently felt confident, and his results prove, that his silver had remained unaltered. In fact, it is quite within the limits of probability that with only ordinary precautions, metallic silver may be kept unaltered not only for decades but even for centuries. Finally, pure metallic silver as the ultimate standard in volumetric analysis would offer the additional advantages that when used in the form of bright sheets, its undiminished brightness could always be taken as a good indication, at least, of its having retained its original purity; while by using comparatively large pieces of it,<sup>22</sup> any possible loss of the standard substance in transferring from the container in which it is weighed to the vessel in which the analysis is carried out, would be entirely avoided.

Urged by such reasoning as the above, the writer has used pure metallic silver as the standard in volumetric analysis for some time past with very satisfactory results. The plan in general is as follows: About 0.5 Gm. of the silver, accurately weighed, is placed in an Erlenmeyer flask of about 200 c.c. capacity, about 10 c.c. of moderately strong (about 32 per cent.) nitric acid are added, and a small funnel is placed in the mouth of the flask to insure against loss of liquid by spiriting. Gentle heat is applied, and when the silver has dissolved, the solution is diluted with about 25 c.c. of pure distilled water and the nitrous acid expelled by heating the solution to boiling.

<sup>21</sup> *Jour. Chem. Soc.*, 58, 561 (1890).

<sup>22</sup> If metallic silver were generally adopted as the ultimate standard in volumetric analysis, it would be feasible to place the silver on the market as coin-like disks of uniform, accurate, and convenient weight, suitable for direct use in standardization; thus saving considerable time in the execution of the latter and further eliminating personal error.

The funnel is then washed and the washings added to the main solution. This solution is then titrated with a thiocyanate solution of about  $\frac{N}{10}$  strength, using ferric alum as indicator, thus determining the exact value of the thiocyanate solution. By means of this thiocyanate solution, a tenth-normal silver nitrate solution is prepared; and the latter is then used in preparing  $\frac{N}{10}$  HCl. By means of this HCl,  $\frac{N}{10}$  alkali is prepared; and by means of the latter, an oxalic acid solution is standardized. The latter is then used in standardizing the permanganate solution; and by means of the permanganate solution,  $\frac{N}{10}$  sodium thiosulphate is prepared, the process being essentially the same as that given in the U.S.P., only substituting the permanganate in place of the dichromate; the reason for choosing the  $\text{KMnO}_4$  for this purpose, instead of the dichromate, being that a sharper end reaction may be obtained and, as pointed out by Bruhns,<sup>23</sup> the former has also the advantage in that the reaction is practically instantaneous. This, therefore, would give us all the necessary solutions on which is based the entire system of volumetric analysis as usually carried out.

In this connection it is also interesting to note that Rothmund and Burgstaller<sup>24</sup> have recently shown that in shaking the  $\text{AgCl}$  suspension with ether, in determining chlorides by means of the Volhard thiocyanate method, filtration of the  $\text{AgCl}$  is rendered unnecessary, and accurate results are obtained by direct titration of the unfiltered mixture even when the amounts of chlorine are small. And as further showing the advantages of metallic silver as the standard in volumetric analysis, we may mention the recent work of Gooch and Perkins,<sup>25</sup> who showed that free iodine in solution may be accurately determined through its reaction with metallic silver. Likewise, Hopfgartner<sup>26</sup> has shown that potassium permanganate may be standardized directly by means of metallic silver by dissolving the latter in ferric ammonium sulphate which has been acidified with sulphuric acid and titrating the ferrous salt thus formed with the permanganate solution. Finally, when we recall the present commendable tendency to refer all important work to exact standards, as may be illustrated by the work of the Hygienic Laboratory in furnishing the standard for the preparation of the

<sup>23</sup> *Jour. Chem. Soc.*, 90, ii, 577 (1906).

<sup>24</sup> *Zeit. anorg. Chem.*, 63, 330-6 (1909).

<sup>25</sup> *Ibid.*, 318-324.

<sup>26</sup> *Jour. Chem. Soc.*, 88, ii, 484 (1905).



antidiphtheric serum of the U.S.P., it would seem that by adopting pure metallic silver as the ultimate standard in volumetric analysis we would pave the way for finally having such standard supplied from one source, thus making the uniformity absolutely complete. It would seem advisable, therefore, that in the next revision of the U. S. Pharmacopœia pure metallic silver be adopted as the ultimate standard for the required volumetric solutions.

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# A NOTE ON THE SUBSTITUTION OF ANHYDROUS SODIUM SULPHITE FOR THE HYDRATED VARIETY GIVEN IN THE U. S. PHARMACOPŒIA.

BY ELIAS ELVOVE.

According to the present U. S. Pharmacopœia sodium sulphite ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ) should contain not less than 94 per cent. of this salt. The experience in this laboratory, however, has been that when this salt is obtained commercially it frequently contains sulphate as an impurity which is about as large in amount as the remaining sulphite. An idea as to the amount of sulphate which may be present in such samples of sulphite may be obtained from the results of an analysis<sup>1</sup> carried out in this laboratory on a sample of this salt which was obtained from one of the most careful and reliable firms in the country. This analysis resulted as follows:

	Found (Per cent.)
Sodium sulphite .....	22.05
Sodium sulphate .....	25.00
Water (loss on drying in vacuo at 100° C.) .....	52.50
	<hr/> 99.55

That this sample of sodium sulphite probably was up to the required standard when first prepared, but had been thus reduced in its sulphite content as the result of the lapse of time between its preparation and analysis, is indicated by the fact that a sample of this salt ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ) which was prepared in this laboratory and

<sup>1</sup> Kastle and Elvove: *Jour. Infectious Diseases*, 6, 619-629 (1909).

which on analysis immediately after preparation showed a percentage purity of 99.69, was found to have lost approximately one-fifth of its total available sulphite after standing for six months in a glass-stoppered bottle, under ordinary conditions, the bottle having been opened only a few times during this interval in order to remove small amounts of the salt. It appears also that others have met with similar experience in the examination of this salt. Thus

TABLE I

*Showing the Degree of Purity of Samples of Anhydrous Sodium Sulphite Obtained from Various Sources.*

Number of sample	Amount taken for analysis (gramme)	$\frac{N}{10}$ Iodine required (c.c.)	Percentage purity
1 (Commercial) . . . . .	0.1260	18.25	91.25
2       "       . . . . .	0.1260	18.75	93.75
3       "       . . . . .	0.1260	19.20	96.00
4       "       . . . . .	0.1260	19.30	96.50
5       "       . . . . .	0.1260	19.30	96.50
6       "       . . . . .	0.1260	19.45	97.25
7 (Prepared as described by Kastle and Elvove) . . . .	0.1260	19.80	99.00
8 (Prepared and analyzed by Hartley and Barrett, using an indirect method of analysis) . . . . .	0.1260		99.87

Smith, Kline and French Co.<sup>2</sup> report on the examination of 12 samples of sodium sulphite ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ) several of which contained only 90 per cent. of this salt. Likewise, Patch<sup>3</sup> has found all of the four samples which he examined to contain an excess of sulphate; his results showing that 100 parts of the dried sodium sulphite represented from 137 to 167 of the crystallized salt, whereas, if the latter had been of U.S.P. purity, 100 parts of the dried sulphite should have contained enough  $\text{Na}_2\text{SO}_3$  to represent about 188 parts of the crystallized salt.

<sup>2</sup> Lab. Rep., S. K. and F., 1906, p. 20; from Bull. No. 58, Hyg. Lab., U. S. Pub. Health and Mar. Hosp. Ser., Wash., p. 481.

<sup>3</sup> Proc. A. Ph. A., 54, 346 (1906).

On the other hand, anhydrous sodium sulphite was found, by Hartley and Barrett,<sup>4</sup> to be stable so long as it is kept dry, while Kastle and Elvove<sup>5</sup> also found the anhydrous salt to show practically no change even when kept under ordinary conditions in glass-stoppered bottles for about a month. The latter authors have also pointed out<sup>6</sup> the advantage that is gained by the use of anhydrous sodium sulphite in place of the hydrated salt in the preparation of Endo's<sup>7</sup> medium, and in this connection have also described a modification of Hartley and Barrett's method for the preparation of anhydrous sodium sulphite which increases the yield and makes it of greater general convenience to carry out. Likewise, the marked difference in the stability of anhydrous sodium sulphite, as compared with the hydrated salt ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ), may be seen from the results obtained in the examination of commercial samples of these salts. Thus, a sample of the anhydrous sodium sulphite, obtained from the same firm that supplied the hydrated sodium sulphite which, according to the analysis above mentioned, contained only 22.05 per cent. of  $\text{Na}_2\text{SO}_3$ , was found to be 96.5 per cent. pure  $\text{Na}_2\text{SO}_3$ . In fact, even the poorest of the samples of anhydrous sodium sulphite examined was found to contain over 91 per cent. of available  $\text{Na}_2\text{SO}_3$ , as may be seen from the results given in Table I.

That the anhydrous sodium sulphite remains practically unaltered, even when kept for a comparatively long time, under ordinary conditions, in glass-stoppered bottles, may be seen from the results given in Table II.

These results show, therefore, that even after having stood for over seven months, under ordinary conditions, in glass-stoppered bottles, none of the samples of anhydrous sodium sulphite examined, altered in its available sulphite to an extent which might be considered practically significant when compared with what takes place, under similar conditions, in the case of the hydrated salt. It would seem advisable, therefore, that in the next revision of the U.S.P., anhydrous sodium sulphite be substituted for the hydrated variety given in the present U.S.P.; and as the results given in Table I show that several firms now supply anhydrous sodium

<sup>4</sup> *Jour. Chem. Soc., Trans.*, **95**, 1178-85 (1909).

<sup>5</sup> *Loc. cit.*

<sup>6</sup> *Loc. cit.*

<sup>7</sup> *Centralbl. f. Bakt., Orig.*, 1903-4, **35**, p. 109.

sulphite in a condition of purity representing over 96 per cent. of the theory, it would seem that a minimum purity requirement of about 95 per cent. of the theory would certainly not be unreasonable.

In this connection it may also be noted that while the primary reason for the desirability of substituting the anhydrous sodium sulphite for the hydrated variety given in the U.S.P. is the great difference in their stability under ordinary conditions, there is also

TABLE II  
*Stability of Anhydrous Sodium Sulphite.*  
(Kept under ordinary conditions, in glass-stoppered bottles.)

Number of sample	Length of time kept (days)	Amount taken for analysis (gramme)	$\frac{N}{10}$ Iodine required (c.c.)	Percentage purity
1	1	0.1260	18.25	91.25
1	221	0.1260	18.00	90.00
2	1	0.1260	18.75	93.75
2	221	0.1260	18.60	93.00
3	1	0.1260	19.20	96.00
3	221	0.1260	18.85	94.25
4	1	0.1260	19.30	96.50
4	221	0.1260	18.95	94.75
5	1	0.1260	19.30	96.50
5	221	0.1260	19.05	95.25
6	1	0.1260	19.45	97.25
6	221	0.1260	19.30	96.50
7	1	0.1260	19.80	99.00
7	221	0.1260	19.60	98.00

an economic reason favorable to such change. For, inasmuch as the activity or value of the sodium sulphite depends entirely on the amount of available  $\text{SO}_2$  which it contains, and as we can readily see that the latter would constitute a proportionately larger amount in the anhydrous salt than in the hydrated, the proposed change would, therefore, result in considerable saving in the cost of transportation. Thus a pound of the sodium sulphite of the U.S.P. ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ), even when absolutely pure, has only about half



the amount of available  $\text{SO}_2$  which is available in an equal weight of the anhydrous salt,  $\text{Na}_2\text{SO}_3$ ; or perhaps we may better illustrate this point by taking the actual case of the firm referred to above, from whom samples of each of these salts were obtained. The transportation charges for equal weights of these salts would ordinarily be equal; although the amount of available sulphite,  $\text{Na}_2\text{SO}_3$ , in the hydrated salt was only 22.05 per cent. of its weight whereas in the anhydrous salt it was 96.5 per cent. of its weight, thus making the cost of transporting the sulphite of the former over four times its corresponding cost in the latter case. Besides, the cost of the anhydrous salt was less than twice the cost of an equal weight of the hydrated salt, although on the basis of the available  $\text{SO}_2$  the former is worth double the price of the latter, even if both were of an equal degree of purity; thus actually making the anhydrous salt a cheaper source for  $\text{SO}_2$  than the corresponding hydrated salt, even if we do not consider the difference in the cost of transportation; while if the manufacture of the anhydrous salt were based on the principle on which rests the method of Hartley and Barrett,<sup>s</sup> namely, that crystallization of the anhydrous sulphite is obtainable by boiling its aqueous solution, the cost of the anhydrous salt could probably become reduced to even less than the present cost of the sodium sulphite of the U.S.P. Finally, the anhydrous sodium sulphite has also the advantage over the corresponding hydrated salt in that it is more suitable for the exact weighing of prescribed amounts, such as are required in the making of certain preparations, or for yielding previously calculated amounts of  $\text{SO}_2$ .

Inasmuch, however, as the disadvantage of instability applies also to the acid sodium sulphite or bisulphite,  $\text{NaHSO}_3$ , which is included in the present U.S.P.; and perhaps with even greater force, on account of its apparently higher degree of instability, as was indicated by an experiment tried in this laboratory, and as is also indicated by the fact that the U.S.P. purity requirement for this salt is only 90 per cent. against 94 per cent. in the case of the corresponding normal salt,  $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ; it appears desirable, therefore, to avoid, if possible, the inclusion of the acid salt in the U.S.P. as a substance having a fixed standard of purity. In fact, there appears no sufficient reason why the acid sodium sulphite might not be omitted entirely from the list of official substances, since the

<sup>s</sup> *Loc. cit.*

normal salt probably could replace it in most cases; and where it could not replace it directly it might replace it indirectly by using it in conjunction with an equivalent amount of a suitable acid, as hydrochloric, sulphuric, or sulphurous acid. Of course when we compare the concentration of the available  $\text{SO}_2$  (25.4 per cent.) in the sulphite ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ) with that in the bisulphite (61.5 per cent.), the difference in favor of the latter is quite large, thus rendering it of especial value in all cases where a high concentration of available  $\text{SO}_2$  is required; but when we remember that by substituting the anhydrous sodium sulphite for the hydrated sulphite of the U.S.P. we also double the concentration of available  $\text{SO}_2$ , the difference in favor of the bisulphite becomes practically negligible. Thus the bisulphite of the U.S.P. (90 per cent. purity) would have a concentration of available  $\text{SO}_2$  equivalent to about 55 per cent., whereas the anhydrous sodium sulphite (over 96 per cent. purity in many commercial samples) would have a concentration of available  $\text{SO}_2$  equivalent to about 49 per cent.; the difference in the concentration of available  $\text{SO}_2$  in the latter case, therefore, could hardly affect the reaction in any given case where the bisulphite might be used as a reagent.

On the other hand, it seemed that, having the anhydrous sodium sulphite as a ready source of supply of  $\text{SO}_2$ , we might also be able to readily prepare and isolate the bisulphite whenever wanted by taking advantage of the comparatively sparing solubility of the latter in strong alcohol. In order to test this plan the following experiment was tried:

Since 1 Gm. of water will absorb<sup>9</sup> 0.168 Gm. of  $\text{SO}_2$  (at  $8^\circ \text{C}$ . and a barometric pressure of 760 mm.), to saturate 40 Gm. of water would require 6.72 Gm.  $\text{SO}_2$ . To obtain this quantity of  $\text{SO}_2$  from  $\text{Na}_2\text{SO}_3$ , 13.2 Gm. of the latter will be required. Since, however, the actual amount of  $\text{Na}_2\text{SO}_3$  in the sample of sulphite used was only about 95 per cent., it would, therefore, theoretically require 13.9 Gm. of the sulphite. This, therefore, gives us an idea as to the approximate amount of sulphite required under the conditions of this experiment; hence 15 Gm. of the sulphite were used. This was placed in a distilling flask of about 250 c.c. capacity, the mouth of which was fitted with a doubly perforated stopper; one of these perforations being used for connecting with the separatory funnel,

<sup>9</sup> Watts' Dictionary of Chemistry, vol. 4, p. 614 (1902).

into which 30 c.c. of strong (93 per cent.) sulphuric acid were placed; while the other perforation in the stopper was used for uniting, by means of suitable tubing, the inner atmosphere of the flask with that of the separatory funnel; the arrangement, therefore, being the same as that previously used<sup>10</sup> for the preparation of chlorinated soda solution. The delivery tube of the flask was connected with a small Drechsel gas washing bottle, in which were placed 40 Gm. of recently distilled water. The Drechsel bottle was placed in a glass jar containing ice-water and unmelted ice, and its outlet tube was connected with a piece of glass tubing which led into a test-tube containing a little of a strong solution of sodium carbonate. After all the connections had been made, the stop-cock of the separatory funnel was turned so as to let the sulphuric acid fall slowly in drops on the solid  $\text{Na}_2\text{SO}_3$  in the flask. Heat was not applied at the beginning of the operation, but when the current of  $\text{SO}_2$  was observed to have weakened, gentle heating was applied to the flask, and the operation continued until practically the entire available  $\text{SO}_2$  had been evolved. When thus carried out not even the slightest odor of  $\text{SO}_2$  could be noticed in the room in which this operation was performed. The Drechsel and contents were weighed before and after the passage of the  $\text{SO}_2$  into it and the increase in weight was found to be 6.8 Gm., corresponding, therefore, to 8.7 Gm. of sulphurous acid,  $\text{H}_2\text{SO}_3$ . To combine this amount of  $\text{H}_2\text{SO}_3$  with  $\text{Na}_2\text{SO}_3$  so as to yield the acid salt,  $\text{NaHSO}_3$ , it would require 13.4 Gm. of pure  $\text{Na}_2\text{SO}_3$ , or 13.96 Gm. of a sample containing 96 per cent.  $\text{Na}_2\text{SO}_3$ . The latter quantity was, therefore, added to the sulphurous acid solution in the Drechsel, the removable upper part of the latter was replaced by a cork, and the contents well shaken. It was then transferred to a beaker of about 250 c.c. capacity and 200 c.c. of alcohol added to it. The beaker and contents were then placed in the ice-water bath, the contents well mixed, and the whole allowed to remain in this bath for about 15 minutes. The precipitate formed was filtered off on a Hirsch funnel with the aid of the vacuum pump until no more liquid could be observed to drain from the funnel; the final drying being effected by pressing between layers of filter paper. The weight of the bisulphite thus obtained in the solid state was found to be over 11 grammes, representing,

<sup>10</sup> AMER. JOUR. PHARM., 82, 161-166 (1910).

therefore, about 50 per cent. of the theory. The filtrate, however, continued to yield further crops of the salt which, if it had been desired to collect, would have increased the obtained yield still further. An analysis of this salt showed it to be 96.5 per cent. pure sodium bisulphite,  $\text{NaHSO}_3$ .

It is thus seen that when having the anhydrous sodium sulphite we can readily obtain a sulphurous acid solution containing about 14.5 per cent.  $\text{SO}_2$  (the U.S.P. requires not less than 6 per cent.  $\text{SO}_2$ ); and that by adding to such a sulphurous acid solution an equivalent of the solid anhydrous sodium sulphite, we can readily obtain a very strong solution of the acid salt (which could be used as such in at least many cases where the bisulphite is required); while by adding a sufficient amount of alcohol to such an aqueous solution of the bisulphite we can readily obtain the latter even in the solid state and in a condition of higher purity than that required by the U.S.P. It would seem, therefore, that in addition to the substitution of the anhydrous sodium sulphite in place of the hydrated sulphite ( $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$ ) given in the present U.S.P., and the omitting of the acid salt or bisulphite from the list of substances having a fixed standard of purity, it might also be well to substitute anhydrous sodium sulphite as the source of the  $\text{SO}_2$  in the preparation of sulphurous acid instead of obtaining the latter by the indirect, and certainly not very simple, method of reducing sulphuric acid by means of charcoal, which is the method adopted in the present U.S.P.

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## NOTES ON QUININE SALTS AND OTHER CHEMICALS OF THE U. S. PHARMACOPŒIA.

BY GEORGE L. SCHAEFER.

The following notes on the solubilities of a few important quinine salts in ether and other solvents are given, for the reason that there are a considerable number of discrepancies in the literature regarding these data. I have also included a few corrections of the melting points and other tests of a few other chemicals in the U. S. Pharmacopœia, which may be of interest to pharmaceutical chemists at the present time.



QUININE HYDROBROMIDE.

Lines 21 and 22 of the U. S. P. description of this salt read: "Ammonia water added to an aqueous solution of the salt produces a white precipitate, which is soluble in a large excess of the reagent." This test cannot be carried out, except with very small traces of the salt, and ought to be omitted.

In view of this I would suggest the following modification of this test and its adoption for all the quinine salts: "Ammonia water added to an aqueous solution of the salt produces a white precipitate, which is easily soluble in ether." This would differentiate the quinine salts at once from the salts of other cinchona alkaloids.

The solubility in ether of this salt is, according to the U. S. P. 1 to 16, while it is practically insoluble or very difficultly soluble, requiring about 700 parts of the solvent for solution.

QUININE HYDROCHLORIDE.

According to the U. S. P., sulphuric acid should not produce a color with this salt. However, if the salt is treated with concentrated sulphuric acid the resulting solution is yellowish, hydrochloric acid gas being developed.

When slowly heated it melts at about 120° C. with its full amount of water of crystallization. The commercial salt containing 1-2 per cent. less water melts at about 125° C. The completely anhydrous salt melts at about 155-160° C. The latter quickly absorbs water from the air, again lowering the melting point.

There is no distinct melting point for the commercial salt, according to the larger or smaller percentage of water of crystallization in the salt, the melting point differing from 5-10° C.

The salt is not soluble in ether in the proportion of 1 to 240, but it is almost insoluble or very difficultly soluble in ether, requiring about 1000 parts of the solvent.

QUININE SALICYLATE.

Solubility in water at 25° C.....	1:2100
Solubility in water at 80° C.....	1:280
Solubility in alcohol at 25° C.....	1:23
Solubility in alcohol at 60° C.....	1:5
Solubility in ether, about.....	1:780
Solubility in chloroform.....	1:10

## CODEINE ALKALOID.

The solubility of this alkaloid in ether is not 1 to 12½, but 1 to 25.

## CODEINE PHOSPHATE.

All the preparations on the market contain only ½ molecule of water of crystallization. The salt with 2 molecules of water exists, but it is a practical impossibility to produce it for commercial purposes.

The salt with ½ molecule of water ought to be made official, being the pure commercial chemical.

## DIACETYL MORPHINE HYDROCHLORIDE.

In all the publications pertaining to this salt the formula is written  $C_{17}H_{17}(C_2H_3O)_2NO_3HCl$ , this having reference to the anhydrous salt, which, however, cannot be made commercially. The salt, when freshly prepared from an alcoholic solution in the regular way and dried in the air, contains 3 molecules of water of crystallization. When dried at a moderate heat it becomes anhydrous, but if this anhydrous crystalline powder is taken from the drying room it absorbs quickly 1 molecule of water of crystallization from the air. Therefore, no anhydrous salt can be found on the market. The following formula ought to be adopted for this chemical:  $C_{17}H_{17}(C_2H_3O)_2NO_3HCl + H_2O$ , which accordingly contains 95.75 per cent. of anhydrous salt and 4.25 per cent. of water of crystallization, and which is the pure commercial salt.

## STRYCHNINE ALKALOID.

Solubility in alcohol at 25° C. .... 1:150

Solubility in chloroform at 25° C. .... 1:7

## STRYCHNINE NITRATE.

Solubility in water at 25° C. .... 1:55

Solubility in alcohol ..... 1:220

## STRYCHNINE SULPHATE.

Strychnine sulphate does not melt at 200° C. If heated to about 250° C. it begins to get brown, and at a higher temperature it

melts with decomposition. It thus follows that no distinct melting point can be given for this salt.

Solubility in water at 25° C.....	1:45
Solubility in water at 80° C.....	1:9
Solubility in alcohol at 25° C.....	1:105

SALICYLIC ACID.

This acid requires 475 parts of water at 25° C. for solution.

ACETPHENETIDIN.

The test adopted by the U. S. Pharmacopœia for the determination of the presence of acetanilide cannot be used in its present form, as even the purest acetphenetidin will not give a clear solution. If, however, the method is modified in the following way, very small quantities of acetanilide can be detected:

A quantity of 0.1 Gm. of acetphenetidin is mixed in a test-tube with 2 c.c. of a solution of potassium hydroxide, 1 to 2, and the test-tube put in boiling water for two minutes, shaking it during this time. The contents of the tube are now diluted with 4 c.c. of cold water, the mixture cooled and filtered through a small pellet of glass wool. To the resulting clear liquid 5 c.c. of solution of chlorinated soda are added. If the acetphenetidin is pure a clear yellowish solution is produced; if acetanilide is present the liquid will assume at once a slight to a dark purplish-brown color, according to the quantity of acetanilide present, the color changing gradually to yellow when allowed to stand for some time.

This test will show the presence of even less than 2 per cent. of acetanilide.

A list of official chemicals is appended for which the sulphuric acid test has been adopted. It is very important to have this test carried out in distinct proportions of the substance and concentrated sulphuric acid to get uniform results in the hands of different chemists. From practical experience I have found the proportions given in this list to be perfectly satisfactory.

PROPOSED PROPORTION OF SUBSTANCE AND CONCENTRATED  
SULPHURIC ACID.

Atropine .....	0.02 : 5	c.c.
Benzoic acid .....	1 : 10	c.c.
Caffeine .....	0.1 : 10	c.c.
Cinchonidine sulphate .....	0.1 : 10	c.c.
Cinchonine sulphate .....	0.1 : 10	c.c.
Cocaine hydrochloride .....	0.1 : 10	c.c.
Codeine alkaloid .....	0.1 : 10	c.c.
Codeine phosphate .....	0.1 : 10	c.c.
Codeine sulphate .....	0.1 : 10	c.c.
Hyoscyne hydrobromide .....	0.01 : 5	c.c.
Hyoscyamine sulphate .....	0.01 : 5	c.c.
Hyoscyamine .....	0.01 : 5	c.c.
Morphine .....	0.1 : 10	c.c.
Physostigmine sulphate .....	0.01 : 5	c.c.
Physostigmine salicylate .....	0.01 : 5	c.c.
Pilocarpine hydrochloride .....	0.01 : 5	c.c.
Pilocarpine nitrate .....	0.01 : 5	c.c.
Piperine .....	0.1 : 10	c.c.
Quinine .....	0.1 : 10	c.c.
Quinine bisulphate .....	0.1 : 10	c.c.
Quinine hydrobromide .....	0.1 : 10	c.c.
Quinine hydrochloride (slightly yellow) ..	0.1 : 10	c.c.
Quinine sulphate .....	0.1 : 10	c.c.
Sparteine sulphate .....	0.01 : 5	c.c.
Strychnine .....	0.1 : 10	c.c.
Strychnine sulphate .....	0.1 : 10	c.c.

LABORATORY NEW YORK QUININE AND CHEMICAL WORKS.



## THE ASSAY OF OINTMENT OF AMMONIATED MERCURY.

BY JOHN R. RIPPETOE.

Determining the ammoniated mercury by extracting the fats by means of a volatile solvent and collecting the insoluble residue of this salt on balanced filters, or a Gooch crucible, proved to be very tedious and besides it was impossible to obtain a result that was even approximate. Ether, petroleum ether, and chloroform were the solvents used. Several filter papers of fine texture were used, but none of them seemed to be of such a character as to prevent some of the ammoniated mercury from being carried through. Extraction of the fats by means of a Soxhlet apparatus, using an extraction tube, was even less satisfactory.

Hence the following method was worked out which so far has given very satisfactory results. Weigh accurately 2.5 to 3.0 grammes of the sample into a four-ounce, wide-mouthed Erlenmeyer flask. Add 50 c.c. ether and dissolve the fats by agitation, then add 10 c.c. hydrochloric acid (10 per cent.) and 10 c.c. distilled water, and dissolve the ammoniated mercury by agitation. Transfer the solutions to a separator and draw off the acid solution. Wash the flask and separator with water until the washings give no test with silver nitrate solution for chlorides. Pass hydrogen sulphide into the combined acid solution and washings until saturated, and set aside for 15 minutes in a warm place. Collect the mercuric sulphide on balanced filters or a Gooch crucible, wash thoroughly with water, and dry to a constant weight at 100° C. The weight of mercuric sulphide obtained multiplied by 1.0837 equals the weight of ammoniated mercury in the sample taken. Working with a known amount of ammoniated mercury incorporated with the same proportion of white petrolatum and hydrous wool fat, as in the official ointment, 99.1 per cent. of the salt taken was determined, assuming the salt to have been 100 per cent. pure.

The above method should be equally applicable for the assay of the ointments of mercuric nitrate, and yellow and red mercuric oxide.

It would seem desirable that the next revision of the U. S. Pharmacopœia should have some such method of assay for the above ointments, since the present one gives a method of assay for mercurial ointment.

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ECHINACEA AND A SPURIOUS ROOT THAT APPEARED  
IN THE FALL OF 1909.

BY JOHN MOSER, JR., P.D.

Pharmacognosist for J. L. Hopkins &amp; Co.

During the fall of 1909, a root of uncertain botanical origin was offered as echinacea to the New York drug merchants. The commercial source was St. Louis, and for a time nearly all of the echinacea offered was found on examination to be spurious. The spurious root may have been offered before this time, but if so it has not to our knowledge been reported.

A search of the literature on the subject, which is not abundant, failed to bring out any information that would indicate that the root in question had been previously recognized as spurious, or that would throw any light whatever on its probable botanical source. (See note.)

The spurious root when in the entire state differs in certain features from echinacea, but yields a powder that has a very similar appearance, and in this form its detection is extremely improbable without a microscopic examination.

Considerable difference of opinion as to the medicinal value of echinacea exists, as certain recent reports indicate. That the drug is attracting much attention is shown by the fact that the demand is constantly increasing, while the market supply of the true root is now practically exhausted.

Echinacea contains 1 per cent. or more of an acrid resinous substance, and is said also to contain an alkaloid. When tasted it exhibits certain characteristics which would lead one to believe it is far from inert. However this may be, it is certain that the spurious root cannot be expected to represent in any way the activity of the true drug.

A comparative study of echinacea and the spurious root has been made in our laboratory, with a view of bringing out data which will aid in the detection of the spurious when in powdered form or when present as an admixture with powdered echinacea. The principal difference was found in the sclerenchymatous tissue as will be later pointed out.

Two closely related plants of the *Compositæ* contribute to the

supply of echinacea root: *Brauneria purpurea*, the purple cone flower, and *Brauneria pallida*, pale purple cone flower, the former growing from Western Pennsylvania and Virginia to Illinois and southward, and the latter from Illinois and Wisconsin southward. They are perennial herbs with stout and nearly simple stems, terminated by a single large head. The name cone flower is derived from the conical torus, which is covered with a lanceolate, spiny-tipped chaff, longer than the disk florets. The ray florets are about 5 cm. long, drooping, pistillate but sterile, and usually rose-purple in color.

The dried root is the part used medicinally, and has the following characteristics: Root of vertical growth, usually in pieces 5 to 20 cm. long, 0.5 to 3 cm. in diameter; crown branched, the branches somewhat annulate above and with stem scars, rarely stem remnants present; dark brown to blackish externally, slightly tapering, sometimes twisted, deeply longitudinally wrinkled; fracture short, weak; bark thin, 0.5 mm. or less in diameter, and brownish; wood radiate from the numerous greenish-yellow wood wedges; parenchymatous tissue dark gray to blackish; odor distinctly and peculiarly aromatic, characteristic; taste pungent, somewhat acid, producing a profuse flow of saliva, followed by a tingling sensation and slight numbness.

The powder may be described as follows: Light grayish-brown; tracheæ numerous, lignified, 15 to 20 $\mu$  in diameter, with simple pores, or 20 to 50 $\mu$  in diameter and scarlariform; wood fibres usually single or in groups of 2 or 3, 250 to 600 $\mu$  long, 20 to 30 $\mu$  in diameter, the average being 300 $\mu$  long and 25 $\mu$  in diameter, strongly lignified and with numerous simple pores; cork cells irregular and deep reddish-brown; parenchyma of cortex irregular and with yellowish- or reddish-brown resinous contents; fragments of resin cells with suberized walls and a pale yellowish resin which is changed to greenish-yellow by KOH, breaking up into small globules and apparently dissolving. When mounted in concentrated H<sub>2</sub>SO<sub>4</sub> the fragments of parenchymatous tissue assume a reddish-brown color which gradually deepens. Stone cells are absent.

The spurious root has the following characteristics: Somewhat conical crown, 3 to 10 cm. long, 1 to 4 cm. in diameter, tapering upward and terminated by a stem scar or stem remnant; dull brown to blackish externally and finely wrinkled; base spherical and giving rise to several fusiform roots of horizontal growth, 5 to 15

cm. long, 0.5 to 2 cm. in diameter, dark brown to blackish externally and longitudinally wrinkled; occasionally with fibrous rootlets, sometimes also fusiform, and 5 to 10 cm. long; fracture short-fibrous, rather tough; bark 0.5 to 1 mm. thick, brownish and with numerous groups of stone cells; wood grayish, radiate with yellow wood wedges; odor faintly but distinctly aromatic; taste momentarily pungent, slightly bitter and acid.

The powder is light gray in color and also exhibits the following characteristics: Tracheæ numerous, lignified, 15 to 50 $\mu$  in diameter, with simple or bordered pores, occasionally with scarlariform markings; wood fibres 200 to 300 $\mu$  long, 12 to 30 $\mu$  in diameter, strongly lignified and with simple pores; stone cells numerous, usually in groups, isodiametric and 25 to 40 $\mu$  in diameter, or elongated, 50 to 150 $\mu$  long, 25 to 40 $\mu$  in diameter, very thick walled and with numerous simple pores; cork cells reddish-brown; parenchyma of cortex regular and with a brownish or reddish resinous content; fragments of resin cells with pale yellowish resin, less numerous than in echinacea. KOH and concentrated H<sub>2</sub>SO<sub>4</sub> have an action similar to that on echinacea.

In the examination of powdered echinacea containing some of the spurious root, the isolation of the sclerenchymatous fibres by means of Schultze's macerating solution or by digestion with 10 per cent. KOH solution, was found to facilitate the work greatly and to render it possible to detect minute quantities of the spurious root.

NOTE.—Since the completion of this article the attention of the author was called to the editorial "Is Echinacea Valueless" in *The Druggists' Circular*, February, 1910, p. 70. It is stated that a St. Louis friend of the editor called attention to the fact that a large quantity of the root of *Parthenium integrifolium* had been collected in that vicinity and disposed of in the St. Louis market. He also expressed the fear that it was intended as a substitute for or adulterant of echinacea. From the brief description which is given of parthenium it would appear that its characteristics are very similar to, if not identical with, the spurious root herein described. However this cannot be definitely stated until an opportunity is afforded to examine an entire plant at the flowering period.

It is believed that the facts here presented will enable the manufacturer to insist upon being supplied with the true echinacea, the identity of the spurious root being of secondary importance.



## RAPID CHEMICAL FILTRATION COMPARED TO SLOW SAND FILTRATION.

BY WILLIAM G. TOPLIS.

On three previous occasions <sup>1</sup> it has been my privilege to address this body on the subject of water purification—each time some phase of slow sand filtration was considered.

To-day the subject is again water purification, but this time we consider a different side, which is known as rapid filtration. In order that we may have a better understanding of the difference between the two methods, it seems proper to restate, briefly, the basic principles of slow sand filtration. This method is favored for the purification of municipal water supplies and the objects sought to be accomplished are: first, the removal of suspended matter, and, second, the decomposition of organic matter in solution. The first is simple, the mud being strained out as the water percolates through the sand. The second is much more complex, and is brought about through the growth of living vegetable organisms, known as bacteria, that thrive within the sand bed, and are attached to the grains of sand, in such quantity that they actually form a coating over the surface of each grain of sand. The sand bed is about four feet deep. The water is controlled in its passage through the sand and is allowed to proceed at a rate of from three to six million gallons per acre per twenty-four hours. This means that each square foot of area filters about ten cubic feet of water in twenty-four hours at the three million rate. Now as the strained water passes through the fine spaces between the grains of sand in the filter it carries the dissolved organic matter together with some atmospheric oxygen, also in solution, to the bacteria growing within the sand bed. Here the organic matter is absorbed by these growths, and it furnishes pabulum for their existence and propagation. The extreme limit of organic contamination in drinking water is perhaps represented in urea, and as the greater includes the less, the treatment of urea will cover all kinds of organic contamination. Urea is composed of four elements: carbon, hydrogen, oxygen, and nitrogen. As the contaminated water passes slowly through the sand the

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<sup>1</sup> AMER. JOUR. PHARM., 74, 67, Feb., 1902; 76, March, 1904; 81, 220, May, 1909.

bacteria absorb the dissolved matter and digest it and resolve it into the simple oxides of the elements composing it, viz., carbon becomes carbon dioxide ( $\text{CO}_2$ ), hydrogen and oxygen combine to form water ( $\text{H}_2\text{O}$ ), nitrogen is finally changed into compounds of nitric acid.

Chemical analyses of water properly treated by the method thus described prove the statements to be facts, and the water wholly acceptable from both hygienic and æsthetic considerations. There is no better method known for the purification of municipal water supplies when properly conducted. It will be noted, however, that the conditions are rigid and inflexible, and that the method is suitable for but one purpose and limited to that one, especially so because of the large areas of land necessary for its execution.

The purification of municipal water supplies is but one of the many water purification problems, which problems seem to be of unending variety, and call for wide knowledge and experience for their successful handling. The variety of requirements for industrial purposes calls for a system of great flexibility, one that can be quickly adapted to changing needs, and deliver large volumes of treated water in little time and by apparatus that must be confined to restricted space. These conditions are quite the reverse of those necessary in slow sand filtration.

There are two types of rapid filtering apparatus, one of the open variety known as the "gravity filter," and one which is closed and constructed in a metallic case, known as a "pressure filter." The closed type is used where filtered water is to be delivered to a level higher than that of the filter, and the open type is used where the water may flow from the filter by gravity to a point of delivery below the level of the filter.

The same principles are involved in the operation of both types; and both types are built on the same general plan though the pressure filter must be provided with a cover bolted upon it. The most common form is that of a cylinder, of any suitable material. It may be of wood, metal, or concrete, provided with proper inlets and outlets. At the bottom, inside of the container, a special line of piping is arranged. Upon the upper surface of this piping a number of sand valves are placed. The sand valve is the most important feature connected with this system of filtration. Its function is to retain the sand in the filter but allow the water to pass freely out after filtration, and in addition to this allow the freest ingress of water

at the bottom of the filter for washing purposes; and, further, the sand valve must be so constructed that it will automatically open and discharge any particles of sand that may effect lodgement in its parts.

The action of these filters is wholly chemical. In the reaction between alum and bicarbonate of calcium is found the agency to which this method owes its efficiency. All river and spring waters have hardness to a greater or less degree, and very few, if any, are devoid of it. Hardness is commonly due to the presence of lime compounds dissolved in the water, generally in the form of bicarbonate of calcium. If a solution of alum be added to such water, being careful to keep the lime compounds in excess, an interchange between the alum and lime follows, with the result that aluminum hydrate is precipitated, carbon dioxide is evolved, and sulphate of calcium produced, the latter remaining in solution. The objective point of this reaction is the production of aluminum hydrate. This substance when freshly precipitated forms a very voluminous, gelatinous, white precipitate that embraces all suspended matter in a sticky envelope and holds it in a layer upon the sand. The water passes through at a rate greatly in excess of the slow sand method, about 100 to 1. So thoroughly is the filtering performed that the water is quite as brilliant as the most carefully prepared distilled water.

The result in this respect is very often better than the slow sand filter attains. This is not surprising when it is remembered that the particles of clay suspended in water are often less in size than bacteria, and frequently are as small as one one hundred thousandth of an inch in diameter, as has been determined by the Massachusetts State Board of Health.

After the filter has been operating for a period it becomes noticeably clogged, resulting in what is technically known as loss in head—to remedy this condition the filter is washed by passing in at the bottom filtered water through the sand valves, at such a rate that the sand is turned over and lumps and adhesions are broken up, and all of the adhering mud and separated matter are washed out of the filter into the sewer. This is accomplished in from five to ten minutes and the filter again performs its duty when the flow of water is directed downward through the sand.

As stated before no oxidizing action takes place in this method of filtration, but recently successful effort has been made to bring

this about in a chemical way as follows: Calcium hypochlorite in solution was introduced into the water before filtration in the proportion of two or three parts per million. The reaction that follows is precisely the same as that employed in urinalysis in the estimation of urea in which nitrogen is evolved as gas. The result of this as compared with the oxidation change in the slow sand filter is, instead of forming nitric acid and increasing nitrates, the nitrogen, as gas, is thrown off and hydrochloric acid is produced, increasing chlorides. Other changes are the same. In addition to this the hypochlorite has the effect of increasing the bacterial efficiency to an extraordinary degree.

Another interesting adaptation of this method of filtration may be cited in conditions such as are met in the Passaic River, New Jersey, at Passaic. The water of the river at this city is black, colored by the refuse discharged into it from the silk dye works at Paterson. In addition to the dye, all of the sewage of the City of Paterson empties into this stream, forming a malodorous combination. The problem was to deodorize and decolorize the water and to free it from bacteria to a large degree. The first was accomplished by aeration and sedimentation. The second by taking advantage of the property of aluminum hydrate to form lakes with dye colors, that, becoming insoluble in water, are easily filtered out and these, together with the bacteria, were readily removed by the filter, working at a rate of 1000 cubic feet of filtered water per square foot per twenty-four hours. The water resulting from this treatment was suitable for use in bleaching white goods and the manufacture of white paper.

Another problem quite different was met in the treatment of the water supply at Fort Hancock, Sandy Hook, New Jersey. This water was so strongly impregnated with iron that it was altogether unfit for drinking. Tea was turned into ink, and for laundry purposes it was impossible. The Government engineers had endeavored to free it by oxidation and sedimentation, but it was found that all of four days were required for oxidation and not less than two weeks were necessary for complete sedimentation, conditions that were altogether impracticable. Finally, the chemical filter was installed. The water was treated with small quantities of calcium hydroxide in solution and then filtered at the rate of 400 million gallons per acre per twenty-four hours, which is equal to 10 cubic feet in twelve minutes per square foot of surface as compared with



10 cubic feet in twenty-four hours which is the slow sand filtering rate for each square foot of surface. The result was a water entirely palatable and faultless for laundry work.

Each of the preceding examples described applications of principles with the effluent as the objective. The following case is one where the filtered water is run to waste in the sewer and the contamination saved, just reversing the conditions.

At Mt. Vernon, New York, there is a large silver manufacturing establishment. For various reasons considerable silver finds its way into the wash water used by the silversmiths. This waste is allowed to run into a sedimentation basin where it is treated with sodium chloride, and allowed to subside. The water after standing is pumped into a filter where any suspended matter is caught, and after this process has been carried far enough the filter is washed and the washings returned to the sedimentation basin, and the clear water is again directed into the sewer. The saving to the manufacturers is \$5000 per annum, the cost of which is \$150 for one year's operating expenses.

One other and very important adaptation of rapid filtration is that in connection with so-called water softening. This process consists in removing from the water dissolved salts of calcium or magnesium that may be present. The handling of this matter requires precise manipulation as will be understood from the character of the reactions involved—because excess of the reagents would also produce hardness; hardness it will be remembered is commonly due to the presence of bicarbonate and sulphate of calcium. The first step is to add a slight excess of calcium hydroxide to the water. The result of this is to neutralize the half bound carbonic acid of the bicarbonate of calcium and precipitate it as neutral calcium carbonate. After an interval sodium carbonate solution is added, when any excess of calcium hydroxide is changed to neutral carbonate of calcium and the sulphate of calcium is precipitated also as carbonate—the resulting sodium sulphate remains in solution. After this treatment the water is conducted to a filter where the precipitates are removed and the water is passed on practically free of hardness. This treatment is capable of reducing water of extreme hardness at a very rapid rate, to about 2 degrees of hardness. This is the limit because neutral calcium carbonate is soluble in water to this slight extent; refinement in apparatus is absolutely essential but it is quite practicable in competent hands.

## CONSERVATION AND THE CHEMICAL ENGINEER.\*

BY SAMUEL P. SADTLER.

We have heard much in the last year or two concerning the conservation of our natural resources and we shall, I feel certain, hear much more in the next few years, as the facts elicited from the preliminary studies of the subject come to be understood by the public at large. The importance of the subject will grow correspondingly as the matter is studied by the thoughtful citizen, and his appreciation of it will in time be reflected in the activity of the statesmen at Washington in the proposing of remedial measures.

Conservation let us note, however, represents the third stage in the history of the development of natural resources.

The first stage is exploration or discovery. This is the era of the prospector and has given us in this country some famous episodes. We need only recall the discovery of gold in California in 1849 and the way in which it operated to attract adventurous spirits from the older parts of our country, or the repetition of the same story with the discovery of the rich gold deposits on the Yukon and at Nome in Alaska.

The first discovery of rich petroleum deposits of Western Pennsylvania in the early sixties brought, similarly, multitudes of prospectors or "wildcatters," as they came to be known locally, and this experience has been repeated also from time to time as great petroleum gushers or powerful gas wells have been reported in various sections of the country, resulting in the opening of new fields, as in Ohio, Indiana, Kansas, Texas, and Oklahoma.

The second stage is exploitation, when these lavish gifts of nature are worked with a view mainly of increasing production and usually in a wasteful way with no thought of the exhaustion of the supply.

As illustrations of this stage we need only cite the way in which our coal mines have been worked. In Bulletin 394 of the U. S. Geological Survey (papers on the conservation of mineral resources) we find the statement that "it has been estimated that the actual

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\* Presidential address delivered at the second annual meeting of the American Institute of Chemical Engineers in Philadelphia, Dec. 8, 1909; and reprinted from *Metallurgical and Chemical Engineering*, 8, p. 9, Jan., 1910.

loss or waste sustained through coal left in the mines in conducting mining operations amounts to 50 per cent. of the quantity produced and marketed." Worse than this, when the Anthracite Coal Waste Commission made its report in 1893 they estimated that "for every ton produced one and a half tons were lost."

One of our most valuable gifts of nature is the natural gas, which is associated more or less directly with petroleum. It is a fuel of the greatest value, being nearly pure hydrocarbon in its composition. Yet we find in the same Bulletin of the Geological Survey before referred to the following: "As to the amount of natural gas which is being wasted daily, no accurate statistics have been attempted and the judgment of Dr. I. C. White, State Geologist of West Virginia, may well be accepted to the effect that no less than 1,000,000,000 cubic feet of gas are wasted every twenty-four hours. Of this, undoubtedly the larger part is wasted in the production of oil." This waste, Dr. Day of the Geological Survey says, "practically equals the annual consumption of natural gas reported for 1907. This waste should furnish light for half the urban population of the United States."

The exploitation of our once great timber resources and the resulting denudation of great tracts of land and the evils to the soil which have followed in the train of this ruthless waste have been so graphically portrayed by the U. S. Forestry Bureau and others recently that I need not more than allude to this case of reckless extravagance.

It is not my intention, however, to take up this evening the question of the conservation of our natural resources and the absolute need thereof, as so ably developed in recent reports of the "National Conservation Commission," the Forestry Bureau, and other official publications, nor yet the part played by the chemist in this conservation of natural resources which has been so ably reviewed by Dr. Bogert in his recent Presidential address before the American Chemical Society.

What I would like to do is to indicate that these same three stages of exploration or discovery, exploitation or effort at production, and finally conservation, are to be seen in the history of every great chemical industry, and to point out, that, while it is the part of the chemical engineer to aid in the exploitation step, what is still more important is his part in counselling and indicating how the wholesome influence of conservation can be applied so as to broaden

and extend the scope of the industry, to maintain and add to its remunerative character, and to give it stability and promise of permanence.

Let us illustrate this view by examples, and take first the great petroleum industry to which reference has already been made in speaking of the era of exploration when the petroleum fields were first outlined by the work of the prospector and driller. The second stage of exploitation began to draw upon the help of those who were chemical engineers, in fact if not by title. The development of the distilling and refining processes came first. Starting with the old cheese-box still with its circle of heating grates under it, there was a change, following upon the discovery of the "cracking process" as applied to crude oil, to the present form of cylindrical still with its movable cover to regulate the chilling of the vapors during the latter part of the operation. This simple feature in distilling enables the refiners to get 75 per cent. or more of burning oil from the crude petroleum instead of the 45 per cent. of a normal fractional distillation, while producing a residuum which can be advantageously distilled for paraffin oils.

The proper control of the acid and alkali treatment of the crude distillates, the change from the old forms of presses for paraffin scale to the modern filter press, the introduction of bone-black filtration for reduced oils and residuums all contributed to develop and expand enormously the several parts of the industry to which they were applied. With these improvements in large scale methods went the inauguration of improved testing and analytical methods, so that uniformity of product so essential for sound business development was secured.

Let us turn now to the newer evidence of the work of the chemical engineer in the way of conservation as illustrated in this same industry. The collection and utilization for fuel purposes of the uncondensed gas from the distillation of crude oil is one of the important economies that has been generally adopted. The working up of the sludge-acid and recovery of not only sulphuric acid but of valuable side-products is now a feature of the larger refineries. The introduction of clay filtration to improve the quality of the heavier grades of oils is an important advance as well as a step of economy. The production of gas oils from the less valuable crude oils has also become an important industry, as these are of great value for gas-making and gas-enriching. The more thorough utilization



of residues is also a feature of recent years. From these residues are now made excellent road oils for the aid of the good roads movement. The petroleum pitch is all utilized also, partly for electric light carbons and partly for fuel purposes. Most promising of all, however, is the result, not as yet fully attained, but most certain of solution in the immediate future, viz., the utilization of crude petroleum of the lesser valuable kinds and residuums in internal combustion engines for the development of power.

A second typical industry is that of coal distillation. We have already spoken of the wastage in the mining of coal. It is not necessary here to speak of the corresponding waste in its utilization as fuel. We will speak solely of the distillation of coal. This treatment may be carried out from either one of two points of view, and the exploitation in each case has been pushed with great energy, utilizing all available chemical and engineering skill. The first is the distillation for the manufacture of illuminating gas. While the mechanical side of this process has advanced steadily, particularly after the introduction of regenerative firing and mechanical stoking, the chemical side did not advance so rapidly. While the coal-tar is no longer thrown away, unless it be in very isolated localities, the proper chemical utilization of this tar has lagged behind both in this country and in England. On the other hand, the true conservation of this valuable side-product and the development of its possibilities has advanced in a notable degree in Germany, the home of the coal-tar industry. Here the research chemist and the chemical engineer have gone hand in hand in the building up of a great industry or rather two industries based upon the utilization of the coal-tar, the manufacture of the coal-tar dye colors, and the manufacture of synthetic medical preparations possessing valuable therapeutic characteristics. Besides these most important and highly developed illustrations of conservation, we have, however, some minor utilizations of coal-tar or products from the same that deserve mention. Thus the manufacture of creosote oils for the preservative treatment of wood, the roofing-pitch and tar-paper manufacture and the use of pitch in the biquetting of coal are illustrations of value given to the coal-tar and its products.

The thorough extraction of the ammonia and the impurities like the cyanides from the ammoniacal liquor and the production of commercially valuable products from them is, moreover, an accomplishment in the way of conservation. The utilization, too, of the

gas carbon for the manufacture of electrode carbons, battery plates and for electric light carbons is another illustration of this work.

The second method of distilling coal is that for the production of coke for metallurgical purposes. This has been developed or more properly exploited to such a degree that, according to the "Mineral Resources of the United States," published by the U. S. Geological Survey, the production of coke for the year 1907 was 40,779,564 tons, of which, however, 35,171,665 tons were produced in beehive ovens. In these as is well known, only the fixed carbon of the bituminous coal is saved and all volatile constituents including gas, tar, and ammonia are absolutely wasted. On the other hand, 5,607,899 tons of coke were produced in by-product recovery ovens and the value of the by-products (gas, tar, and ammonia) obtained therefrom amounted to \$7,548,071. It is easy to reckon from this what the loss was on the 35,171,665 tons of coke made in beehive ovens. In fact, the article on "Coal," in Bulletin 394 before referred to says with reference to this, "at the prices which prevailed in 1907, the value of the by-products wasted in beehive coke-ovens was a little over \$55,000,000."

But the result achieved by the chemical engineer in the working of this by-product over represents more than merely saving certain by-products. The gas produced can be separated by the perfect control of the method into "poor gas" for fuel purposes and "rich gas" for illuminating purposes, so that the highest economy or conservation of values is thereby attained.

Another industry in which the chemical engineer has worked first for the purpose of exploitation and later for conservation of material and values is the starch industry. Starch, as we all know, is one of the most widely distributed vegetable products and has always played a great part in the world's supply of food. In Europe, it is potato and wheat starch, in the United States it is corn starch, and in tropical countries it is rice, tapioca, sago, etc., that are the important varieties of this cereal food. Not only has the production of starch been developed, however, for food purposes, but enormous quantities of the starchy substances serve as the starting point in the fermentation industries. Then we have the use of both starch and its alteration product, dextrine, in the textile industries and the production of glucose as the product of the hydrolysis of starch, and the manufacture of nitro-starch and its utilization in the explosives industry. All of these industries have attained a high

degree of perfection by the application to them of a chemical understanding of the nature of starch and its alteration products and the devising of processes by which the several reaction changes could be carried out with exactness and economy. What that means as applied to one single branch of the starch industry, those of us who had the opportunity on the occasion of our meeting last June to go through the works of the Corn Products Company at Edgewater, N. J., can appreciate. The glucose production of the United States in 1907 is stated to have been 800,000 tons, requiring 40,000,000 bushels of corn as raw material. But besides the production of the solid grape-sugar and the liquid glucose for a great variety of uses, the separation of the germ of the corn from the starchy portion has made possible the production on a large scale of corn-oil, a product adapted for a wide range of uses—from soap making to the manufacture of rubber substitute.

Turning now to inorganic chemistry for an illustration, we have a splendid example of the work of the chemical engineer in the direction of conservation in the case of the natural and artificial nitrate industry, to which latter the Germans have already given the expressive name of "air-salpetre." The great source of nitrate for forty or more years past has been the deposits on the west coast of South America, furnishing the so-called Chili salpetre or sodium nitrate. This has been drawn upon increasingly until in 1908 the quantity shipped was 1,730,000 tons, valued at \$87,500,000. But the Chilean deposits are far from being inexhaustible. It is estimated that if the annual consumption increases merely by 50,000 tons, and this is to be reasonably expected, from thirty to forty years will see the practical exhaustion of this supply. So in 1899, Sir Wm. Crookes startled the industrial world by calling attention, in what the newspaper men would call a "scare-article," to the nitrogen problem and the necessity of maintaining a supply of nitrogenous plant food if the world's food requirements were to be met. Crookes pointed out the way of relief when he said "the fixation of atmospheric nitrogen is one of the greatest discoveries awaiting the ingenuity of chemists. It is certainly deeply important in its practical bearings on the future welfare and happiness of the civilized races of mankind." The chemical engineer has responded nobly to this demand for conservation of available nitrogenous material by the working out of practical methods for the manufacture of what we called "air-salpetre." It must not be supposed, however, that success was easily obtained.

Not only were the usual experimental difficulties to be overcome but, as Prof. Bernthsen has well shown in his address before the London International Congress of Applied Chemistry in May last, there are theoretical difficulties of the most serious kind standing in the road of ready fixation of atmospheric nitrogen and oxygen in the form of nitrogen oxides convertible into nitrates. So it happened that the first large enterprise of this kind, the process of the Atmospheric Products Company, established at Niagara Falls, had to be given up as commercially unavailable. This was followed by the Birkeland and Eyde process, started in Norway with the cheapest water power to be found, and this is still in successful operation. A few years later (in 1905) the Schönherr process was worked out by the Badische Anilin and Soda Fabrik, also using Norwegian water power and still later the Pauling process at Gelsenkirchen, near Innsbruck, in Tyrol. The Schönherr process seems to be the most successful.

It produces a 40 per cent. nitric acid, calcium nitrate, or calcium or sodium nitrite, according as the absorption part of the process is modified. All of the processes mentioned require the cheapest electrical energy, which can only be developed by cheap water power, and thus far best developed in Norway. Prof. Bernthsen states, however, that probably within a few years the annual output of calcium nitrate or "air-salpetre" will reach 100,000 tons. As this involves first the fixation of atmospheric nitrogen, and second the use of "white coal," as water power is sometimes fancifully called, it is a true lesson in conservation of natural resources, especially as it also enables us to replace a rapidly disappearing natural product.

Closely related to this recently developed inorganic industry of air-salpetre is the slightly older one of calcium carbide and its offshoot the cyanamide or "nitrolime" industry. With the production of calcium carbide in the electric furnace in 1892 by Willson and the publication of Moissan's work on the electric furnace in 1894, sprang into existence a great industry, as the acetylene gas lighting made possible thereby had great advantages. Isolated lighting plants, acetylene lamps for automobiles and carriages, luminous buoys and signals, a new material for lampblack manufacture, and other utilizations all were rapidly developed. The perfecting of the furnaces and the process for this manufacture of carbide enlisted the attention of electrical and chemical engineers and at the present time the world's production of calcium carbide is estimated to be about



200,000 metric tons per annum, largely in countries like Norway, Italy, and Switzerland where cheap water power is available, as well as in the United States at Niagara Falls and Sault St. Marie. This production, however, for the time being outran the demand for carbide for acetylene lighting.

Relief from over-production by finding new outlets and utilizations is always to be preferred to closing of works already in operation, so chemical engineers have found new possibilities for calcium carbide. By far the most important of these is the production from calcium carbide of calcium cyanamide by the action of nitrogen gas, as worked out by Drs. Frank and Caro. We have here an exothermic reaction in which nitrogen is absorbed by the carbide with the production of calcium cyanamide and carbon. This takes place at a temperature of from 800° to 1000° C., much below that needed for the carbide manufacture. Not only can all the nitrogen of this cyanamide be converted into ammonia by decomposition with steam, but it is gradually decomposed by the chemical and bacteriological constituents of the soil into ammonia, which becomes fixed by the vegetable mould and is so held. The cyanamide is also convertible into calcium cyanide by melting with fluxes, into dicyandiamide for dye-color manufacture, into urea, guanidine, and other hitherto relatively expensive organic compounds. The dicyandiamide is already used as a "deterrent" in smokeless powder manufacture, reducing the temperature of the explosion without diminishing explosive force, and the crude calcium cyanamide with certain fluxes under the name of "ferrodur" is employed for case-hardening of iron and steel.

The statement is made that the works for the manufacture of "nitrolime" now in operation or in course of construction have a capacity of 166,000 tons per year.

The illustrations of conservation, whether from the point of view of better utilization of materials, or the production of new and varied products, or the recovery of what were waste products, could be greatly extended did time allow.

We might refer to the way in which sulphur recovery has been worked out in the alkali industry, or to the manganese recovery in connection with the chlorine production from manganese dioxide, so that "recovered manganese" is to-day a most valuable article of commerce. Or we might note the saving resulting from the manufacture of reclaimed rubber, but these and similar illustrations

of the conservation theme as influenced by the work of the chemical engineer will have to be passed by for the present.

That there are numerous problems as yet unsolved of equal and possibly greater importance than some of these discussed will also be conceded by those possessing even a moderate acquaintance with chemical industries.

One of these problems, for instance, is the recovery of the valuable constituents of the waste liquor of the sulphite wood-pulp process. A German authority states that every litre of this waste liquor contains 120 Gms. of organic material as against 10 to 15 Gms. of mineral substance. Dr. A. Frank estimated that in 1904 there was wasted in this way in Germany 300 million kilogrammes of organic material, concerning which we know that it has value in several directions. In this country, the sulphite wood-pulp process has also an extensive development and the same waste liquor is run off into our streams.

A somewhat different problem, but one of even greater importance, is the loss of valuable metals in smelter smoke and fumes. The American production of bismuth is not over 10,000 lbs. a year and considerable amounts of bismuth and bismuth compounds are imported every year. Yet it is estimated in the forthcoming report of the U. S. Geological Survey for 1908 that 880 lbs. of bismuth per day are being thrown off in the smoke of the great Washoe smelter at Anaconda, Mont., and with this also go copper, lead, zinc, arsenic, and other mineral products. One way of saving much of this lost material is pointed out in noting that the replacing of smelting methods by electrolytic methods, possible in some cases, allows these metals to be recovered from the deposited slimes.

In conclusion, let us emphasize the fact that our chemical industries need not merely development or exploitation, but if they are to continue to flourish as we are drawn more and more into international competition they must have the newest and best results of chemical research applied by the experienced chemical engineer. New and better materials must be sought, better processes evolved, economies effected at all possible stages, and waste products carefully looked after. The most successful chemical industries in the world, which show the highest scientific and technical development and which are steadily expanding and throwing out branches, are those of the great German chemical companies. Organizations like the Badische Anilin and Soda Fabrik, which have by their employ-

ment of both research chemists and chemical engineers effected industrial revolutions, one after the other, like the introduction of artificial indigo, the contact sulphuric-acid manufacture, and last of all the production of air-salpetre or artificial nitric acid and nitrates, are those which reap the rich commercial rewards and for the reason that they have done the work and earned them. The hope of a successful American chemical industry lies in the same direction.

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## ABSTRACTS OF THESES ON CHEMICAL SUBJECTS.\*

BY J. W. EHMAN.

PHENYL SALICYLATE (R. J. Wötring).—Chiefly a study of the liquefaction of mixtures of salol with other substances. Salol and menthol may be mixed in the proportion of one molecular weight of the former to three of the latter, also in the proportion of three to two molecules to form a dry powder; two molecules salol to three menthol produce a damp powder and equal molecules of each liquefy.

Salol and camphor in different proportions produce either pasty mixtures or liquids.

Salol with either phenacetine, antipyrin, or salicylic acid will result in dry powders, but the addition of a small amount of camphor to either mixture will cause liquefaction. Salicylic acid with camphor alone forms a dry powder.

Three molecules of salol to one of thymol or one of salol to three of thymol form pasty mixtures; in other proportions they liquefy.

Either one or three molecules of salol to two of chloral hydrate form moist powders, but in other proportions dry mixtures result.

Salol and resorcinol in different proportions form dry powder. With acetanilid a dry mixture results, but the addition of antipyrin causes liquefaction.

Either beta-naphthol, pyrogallol, or sodium salicylate mixed with salol results in dry mixtures. While salol with either antipyrin or resorcinol forms dry powder, when all three are mixed a pasty mass results.

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\* The experimental work embodied in these theses was performed in the chemical laboratory of the Philadelphia College of Pharmacy.

DILUTED NITROHYDROCHLORIC ACID (A. A. Platt).—In view of the time required in its preparation and the poor keeping qualities of the diluted acid, it is recommended that it be prepared when required by simply diluting the strong acid. Six samples were obtained in drug stores, and assayed for free chlorine. One sample, known to have been prepared within a few days, assayed 1.542 per cent. Cl; the others from 0.257 to 0.514 per cent., average 0.334 per cent.

Experiments were made to ascertain the effects of heat in hastening the preparation of the acid. The reaction appeared to be complete in ten or fifteen minutes, and, after dilution, assayed the same percentage of free Cl as an acid made in the usual way and allowed to stand for twenty-four hours before dilution, namely, 1.5 to 2 per cent. The freshly made diluted acid deteriorated rapidly on standing in a warm place exposed to light.

Diluted nitrohydrochloric acid made by diluting some specimens of the strong acid obtained from drug stores assayed from 1.565 per cent. to 5.5 per cent. free Cl.

SOME POINTS OF DIFFERENCE BETWEEN GUM AND WOOD TURPENTINE (S. S. Jacobs).—Specific gravity and refractive index presented no essential difference. As to optical rotation, either gum or wood turpentine may rotate to the right or left, depending upon its source. In carrying out fractional distillation the chief point of difference appears to be that oil from the gum ceases to distil at 165° C., while the wood variety continues to distil up to 185° C., leaving in either case a very small residue. The specific gravity, optical rotation, and refractive index of the different fractions were too variable for definite conclusions to be drawn therefrom. The only distinctive difference between the fractions of the two varieties appears to be the characteristic odor peculiar to each.

SULPHURATED LIME (P. M. Davis).—Of five samples assayed, only one, taken from a sealed package obtained from a wholesale house, contained as much as 55 per cent. calcium sulphide. The author experienced great difficulty in preparing a satisfactory sample from commercial calcium sulphate, but had no difficulty when a chemically pure sulphate was used.

STRAMONIUM (H. W. Eakle).—Leaves were collected from plants, full grown but before flowering, others from plants after flowering but before deterioration, and others were obtained in the wholesale market with time of collection not stated. Tinctures were prepared from the recently dried leaves and were then assayed.



The first specimen assayed 0.0176 per cent. mydriatic alkaloids, the second 0.02048 per cent., and the third 0.0324 per cent.

ZINC STEARATE (C. E. Hoffman).—Of four samples examined, two on ignition left a residue of 15.5 per cent., one 11.4 per cent., and the fourth 9 per cent. The stearic acid liberated from the third had a melting point of 60° C. and that from the fourth was yellow in color and melted at 72° C.

A sample prepared from zinc acetate and soap met the requirements of the U.S.P. A sample prepared by forming a soda soap with the stearic acid and treating this with zinc sulphate produced a satisfactory preparation.

TINCTURE OF IODINE (Ernest A. Noedel).—Analyses of seven samples of tincture of iodine obtained in Philadelphia and vicinity. Iodine per 100 c.c. ranged from 4.522 Gm. to 7.172 Gm., average 6.455 Gm. One specimen, that containing the lowest amount of iodine, contained no potassium iodide. The others contained from 4.08 Gm. to 5.16 Gm. KI per 100 c.c., average 4.67 Gm.

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## CORRESPONDENCE.

### A CORRECTION.

TO THE EDITOR, AMERICAN JOURNAL OF PHARMACY:

Please note, that in the article about "Solubility of Alkaloids, etc.," published in the last issue of your paper, there is a typographical error. Instead of "quinine *hydrophosphite*" it should read "quinine *hypophosphite*." The first named combination, of course, does not exist, and the error ought to be corrected.

Very truly yours,

GEORGE I. SCHAEFER.

April 22, 1910.

## PHILADELPHIA COLLEGE OF PHARMACY.

## MINUTES OF THE ANNUAL MEETING.

The annual meeting of the College was held March 28 at 4 P.M. in the Library. The President, Howard B. French, presided. The minutes of the quarterly meeting held January 4, were read and approved. The minutes of the Board of Trustees for December 7, 1909, January 4, and February 1, 1910, were read by the Registrar, and approved.

The President delivered his annual address, from which the following items of information are abstracted.

## PRESIDENT'S ADDRESS.

The condition of the property in general is very good, numerous repairs having been made during the year. The internal telephone system has been repaired, the push buttons having been removed and replaced by a switchboard, so that the phones are now in first class order. The chemical lecture room which lacked proper ventilation has been remedied by placing an electric fan in the southeast corner, which has proved very successful in securing proper ventilation. The hot-house has been completed, and the Professor of Botany and his assistants have added a small addition to it.

The hot-house has been of material advantage in enabling the Professor of Botany to carry over during the winter about 150 interesting economic plants. These have been used as exhibits during the lectures, and have proven of great advantage to the students, enabling them to familiarize themselves with plants yielding official drugs. The Professor has in addition also had access to one of the largest hot-houses near the city, enabling him to exhibit plants of unusual interest to the students.

The Course in Operative Pharmacy has been unusually successful. The time given to laboratory work has been doubled in the Third Year Course, and nearly so in the First Year Course. The Special Course in Dispensing has also been materially increased.

The Course in Commercial Training has been of unusual interest, a number of lectures by men actively engaged in commercial pursuits having been given.

There is an increase of 40 students over the preceding year. In the Chemical Laboratory 85 students from the three classes have been doing individual work, and 29 third year students are doing thesis work. There have been 26 students in Special Chemistry, four of whom felt themselves sufficiently qualified to take positions of profit, and 44 other students are taking special courses.

During the year six active members have died, in the death of two of whom the College has sustained more than an ordinary loss, viz., Mahlon N. Kline and Thomas S. Wiegand.

The continued activity of the Alumni Association is much appreciated and highly commended. At the reunion of the Alumni Association held last May the Class of 1884 presented to the College a weather observatory barometer, which is to be followed shortly by an aneroid barometer. They also established a Memorial Scholarship.

In conclusion the President expresses his appreciation of the efforts of all who have actively co-operated with him, and hopes that the members, the Faculty, and others interested in the prosperity and advancement of the College, will work together in concord and harmony, having but one purpose in view, and that is, the success of the College.

The address was attentively listened to and at its close was warmly applauded.

#### REPORTS OF COMMITTEES.

COMMITTEE ON PHARMACEUTICAL MEETINGS.—The meetings have been held regularly during the year, various members presiding. A number of the members presented papers or addresses and participated in the discussions, and quite a number of others, not members, several of whom were from other cities, also presented papers and took part in the discussions. The minutes have been regularly published in the AMERICAN JOURNAL OF PHARMACY and reports have been furnished the leading drug journals.

Professor Kraemer, who has acted as Secretary of the Committee on Pharmaceutical Meetings for the past ten years, submitted the following letter:

According to Article XI of the By-Laws of the College, "A recorder shall be elected annually at the Pharmaceutical Meeting in May to issue the notices, prepare business, and record the proceedings of these meetings, and

to make selections therefrom for publication in the JOURNAL." While I am willing to act as recorder or secretary up until the meeting in May, I desire to be relieved of this work, and that another recorder be selected at that time. I am not clear from the By-Law whether it is necessary for the recorder to be a member of the Committee or not.

I am willing to serve on the Committee, but desire to be relieved of the details and responsibilities of the work, particularly as the meetings come at a time when I have class-work, and make this statement at this time in order that it may be properly considered.

I may say that while the meetings are not as well attended by the members of the College as they might be, they are a source of great strength to the College, and must serve to stimulate all our members who read the printed reports of them, and besides serve to attract and interest others who are not members of the College.

In conclusion, I may say that it would indeed be unfortunate if these meetings should ever be discontinued or fail to be conducted on the high plane which has characterized them from the time of their inception.

Respectfully yours,

HENRY KRAEMER.

PUBLICATION COMMITTEE.—The AMERICAN JOURNAL OF PHARMACY has been issued regularly during the year. There is an increase in the amount received from advertisers and quite an increase in the amount received from subscribers. This is a gratifying feature, showing that with the advances in pharmacy and allied lines, the JOURNAL is coming to be more appreciated, particularly by analytical workers.

EDITOR'S REPORT.—As a result of the activity of the members of the American Pharmaceutical Association, particularly in the various branches of the association, and also in the various State pharmaceutical associations, some of the best papers that have been contributed to American pharmacy have appeared in the AMERICAN JOURNAL OF PHARMACY during the past year. Some 61 papers have been published, including seventeen on analytical-chemical subjects, five on strictly pharmaceutical subjects, twenty-seven on Pharmacopœial matters and related subjects, others on pharmacognosy, pharmacology, biological subjects, besides biographical and memorial articles. In addition 33 book reviews were published, as also reports of the annual meetings of the American Pharmaceutical Association, the American Medical Association, the National Wholesale Druggists' Association, the British Pharmaceutical Conference, the Twelfth International Congress on Alcoholism, the Sixteenth International Medical Congress, and other associations.



The quarterly review of the progress in pharmacy continues to reflect the advances abroad as well as in this country.

CURATOR'S REPORT.—The Museum is in good condition and has received a number of donations during the year, the following being the donors: Howard B. French, Charles H. LaWall, M. I. Wilbert, Smith, Kline and French Co., D. H. Hage, James P. Lengel, and E. H. Gane. The historical and general collections are growing in number and importance and soon additional case-room will be required.

Acknowledgments of having received certificates of election to honorary membership were received from Surgeon-General Walter Wyman and Professor O. A. Oesterle.

The members went into executive session at 4.30 P.M. and continued in session till 5 P.M., when the following appointments were announced by the President:

DELEGATES TO THE AMERICAN PHARMACEUTICAL ASSOCIATION: Joseph P. Remington, F. E. Stewart, O. W. Osterlund, William McIntyre, and William L. Cliffe.

DELEGATES TO THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION: C. B. Lowe, William E. Lee, William McIntyre, Charles H. LaWall, H. L. Stiles, Joseph P. Remington, F. P. Stroup, Jacob M. Baer, Theodore Campbell, and Charles Leedom.

DELEGATES TO THE NEW JERSEY PHARMACEUTICAL ASSOCIATION: George M. Beringer, C. B. Lowe, Henry Kraemer, H. L. Stiles, and Theodore Campbell.

COMMITTEE ON BY-LAWS: George M. Beringer, Joseph W. England, and C. A. Weidemann.

The resignation of Theodore L. Gamble, associate member, was accepted.

A letter was received from Mrs. Isadora E. Kline acknowledging the receipt of the "In Memoriam" resolutions on the death of her husband, First Vice-president Mahlon N. Kline.

Professor S. P. Sadtler presented to the College on behalf of the family of the late Rev. Dr. Schaeffer a very ancient hydrometer—probably a century old—formerly used by Doctor William Ashmead, a physician and druggist of Germantown. A vote of thanks was tendered the donors.

The report of the Committee on Nominations was read. Messrs. Jacob M. Baer and Theodore Campbell were appointed tellers, who, after a ballot was taken, reported the election of Howard B. French,

President; R. V. Mattison, First Vice-president; Joseph L. Lemberger, Second Vice-president; Richard M. Shoemaker, Treasurer; A. W. Miller, Corresponding Secretary; C. A. Weidemann, Recording Secretary; Joseph W. England, Curator; and Henry Kraemer, Editor. Trustees for three years: Samuel P. Sadtler, William L. Cliffe, Henry Kendall Mulford. Publication Committee: Samuel P. Sadtler, Henry Kraemer, Joseph W. England, Joseph P. Remington, Martin I. Wilbert, Miss Florence Yaple, and Charles H. LaWall. Committee on Pharmaceutical Meetings: Joseph P. Remington, C. B. Lowe, Henry Kraemer, William L. Cliffe, William McIntyre.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

ABSTRACTS FROM MINUTES OF THE BOARD OF TRUSTEES.

*January fourth, 1910.*—Fourteen members were present. The Committee on Announcement reported that another issue of the *Bulletin* would soon be published; and it was suggested that a brief outline of the activities of the College be published therein, also extracts from the special lectures being delivered in the College.

*February first, 1910.*—Fourteen members present. The Committee on Property was authorized to have repairs made to the intercommunicating telephone system. A communication was read from the Athletic Association and they also submitted a petition favoring athletics, which had been signed by 405 students. A general discussion followed, many of the members strongly advocating that the Board of Trustees establish a Department of Athletics in the institution. The letter and petition were referred to a committee for their consideration and report at a future meeting.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

MARCH PHARMACEUTICAL MEETING.

The stated pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday, March 15, 1910, at 3 P.M., Mr. W. L. Cliffe presiding.

A paper by Dr. George L. Schaefer, chemist for the New York Quinine and Chemical Works, Ltd., on "Solubility of Alkaloids of Cinchona Bark and their Salts," was read, in the absence of the

author, by Freeman P. Stroup, Ph.G. (see April number of this JOURNAL, p. 175).

Prof. Joseph P. Remington said that there are several things to be considered in discussing a paper of this kind, and stated that there are a number of methods for determining solubilities, and that investigators find differences in the solubilities of chemicals due to the differences in methods. He advocated the establishment of standard methods for solubilities, melting points, and other constants. He also called attention to the various alkaloidal assay methods, and said that the Pharmacopœia is specific in this respect, as, for example, under *colchicum corm*, where it is stated that the percentage of alkaloid is that obtained "when assayed by the process given below." The subject of solubilities was also discussed by Frederic Rosengarten and Messrs. Beringer and Cliffe.

George M. Beringer, Ph.M., presented "A Note on Cardamom and Oil of Cardamom" (see April number of this JOURNAL, p. 167), and exhibited samples of the genuine oil which had been furnished him by different firms.

In discussing this paper, Professor Remington asked what would be the advantage in introducing the oil of cardamom into the National Formulary, and into what preparations it would enter? He said that cardamom is used on account of the flavor, and if the proposal was to replace the official cardamom fruit by the oil the preparations would not be as satisfactory to physicians. He stated that the essential oils are largely adulterated and prone to deterioration, especially under the varying conditions under which they are kept in pharmacies throughout the country, and stated that it was on account of the deterioration of oils of lemon and orange that the fresh peel had been introduced into the Pharmacopœia.

Mr. Beringer stated that it was not the intention to replace cardamom fruit for use in the tincture, but to furnish an oil for elixirs in order that physicians might have a choice of these. He said that he had been manufacturing elixirs for twenty years in which cardamom oil was used in small quantities and in such manner as to give a blended flavor. Mr. Beringer stated that the keeping quality of the oil appeared to be well established, oils which he had kept for several years under favorable conditions, in a darkened closet, showing no perceptible change.

J. J. Bridgeman, P.D., said that he had been using an oil of cardamom in prescription work which he knew to be at least four

years old, and that it is still of good quality both as regards flavor and odor.

William G. Toplis, Ph.G., presented a paper on "Rapid Sand Filtration Compared to Slow Sand Filtration" (see p. 227) and in this connection exhibited a model of a "sand valve," and demonstrated the chemical process involved in the purification of water by the use of alum. To show the practical efficiency of rapid sand filtration, Mr. Toplis also read a report on a bacteriological and chemical investigation which he had made of the operation of the filter plant recently installed at Plattsburg Barracks, N. Y., by Hungerford & Terry, Inc., of Philadelphia.

Mr. Cliffe stated that in making milk of magnesia with the filtered water of either the Delaware or Schuylkill River, which is ordinarily clear, the preparation has a yellow color, and that the use of distilled water made the process an expensive one for the retail pharmacist. He then inquired of Mr. Toplis whether in his opinion the entire process outlined by him would render the water of such a degree of purity as to fit it for use in the making of milk of magnesia, which question Mr. Toplis answered in the affirmative. Otto W. Osterlund, P.D., spoke of the same difficulty, and stated that he had found it advisable to abandon the manufacture of milk of magnesia.

Mr. Beringer stated that he makes hydrated oxide of bismuth by an inverted percolation process, which he said is in reality a process of dialysis. He remarked on the difficulty of removing the ammonia in the magma by decantation, stating that much less water is required by his process than in the official method, and that a constant layer of water can be kept above the magma until the process is completed by use of the dropping bottle. He stated, also, that he obviates the undue expense connected with the manufacture of this preparation by manufacturing his own distilled water. For the clarification of tap water he suggested the use of magnesium carbonate or light calcined magnesia as a filtering medium, and stated that sometimes the cloudy appearance of the tap water is due to a disturbance of the lining of the pipes. The speaker also pointed out that in the chemical examination of water, it is desirable for the chemist to have a knowledge of the chemical purification undergone by the water, as, otherwise, supposedly objectionable elements, such as chlorine, resulting from the purification, would be considered natural deleterious ingredients.



Others taking part in the discussion of this subject were Professor Remington and Messrs. Boring and Poley.

A paper on "Echinacea and a Spurious Root That Appeared in the Fall of 1909" by John Moser, Jr., P.D., was presented in abstract by Professor Kraemer, the author not being present (see p. 224).

Mr. Toplis called attention to a method which he has been using in the making of *syrup of ferrous iodide*, in which the bright iron wire of the official formula is replaced by reduced iron, the syrup being of a beautiful green color. He stated that the reaction is very prompt, the time required for the combination of iron and iodine in quantities to give 500 c.c. of syrup being eight minutes, the rise in temperature during the reaction being 18° C., and that the entire process may be completed within one hour. In order to overcome the generation of an excessive amount of heat in the making of larger quantities of syrup, Mr. Toplis suggested that a flask of ample proportions be used, that all of the iodine be added to the water first, and that the iron be added in small successive portions with vigorous agitation after each addition, which method, it was claimed, provides for the dissipation of the heat as rapidly as it is generated.

The chairman directed attention to books, manuscripts, pharmaceutical journals, including bound volumes of the AMERICAN JOURNAL OF PHARMACY from 1854 to 1877, and some specimens of drugs and pharmaceutical preparations, which belonged to our late fellow member, J. B. Moore. Professor Kraemer stated that Mr. Francis B. Hays, of New York, had written him stating that he had obtained through the kindness of Mr. Moore's daughter, Mrs. H. H. Watkins, and son, Rev. J. J. Joyce Moore, both of Philadelphia, letters of the late Albert E. Ebert and Prof. John M. Maisch for the Historical Section of the American Pharmaceutical Association, and also that they would be glad to make a similar disposal of the remainder of their father's pharmaceutical collection, and that, accordingly, he had procured the collection for the College. Of the books the following may be mentioned as of special interest: Richerand's Elements of Physiology, English translation, 1823; The American Dispensatory, by John Redman Coxe, M.D., 1831; Jourdan's Pharmacopœia Universalis, English translation, 1833; Notes of Lectures on the Theory and Practice of Medicine delivered at Jefferson Medical College by John Eberle, M.D., 1834; New Conversations on Chemistry by Thomas P. Jones, M.D., 1839; Dial of the Seasons by Thomas

Fisher, 1845; Treatise on the Practice of Medicine by George B. Wood, 1849.

A motion by Professor Remington, seconded by Professor Kraemer, heartily thanking Mrs. Watkins and the Rev. Mr. Moore for their generous donation, was adopted.

FLORENCE YAPLE,  
 Secretary *pro tem.*

## PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.

TO THE MEMBERS OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION:

On the 28th day of June next we hold our thirty-third annual meeting at Buena Vista Springs.

The Membership Committee realize the importance of a large addition to our number this year. Other State associations have been going forward rapidly, and we feel that this should be our banner year, and there is no good reason why it should not be if every member would try to secure at least one new member. The coming year will be an important one in legislative matters.

If every druggist could be informed touching what benefits he may derive by having our Legislative Committee look after our interests, he certainly would come to the conclusion that it is the best investment he makes (and to think, that only two dollars is all that he is required to pay). In addition—he has the proceedings forwarded him without additional cost—and it is self-evident that if he will read them carefully he will be very much benefited in many ways.

No doubt you are well posted as to the text of this letter, but this is only a reminder from the committee as to what we feel is your duty to your brother druggist.

We enclose herewith a copy of a circular letter, which the Executive Committee have sent to all non-members of the association in the State. A little missionary work on your part will materially aid in bringing those in your State within the fold. Will you do it?

Enclosed please find “blank application.” If in need of more, write our Secretary, Mr. Heffner, or myself.

Yours fraternally,  
 WM. E. LEE.



SOME OF THE OFFICERS OF THE U. S. PHARMACOPŒIAL CONVENTION, MEMBERS OF THE BOARD  
OF TRUSTEES, AND MEMBERS OF THE COMMITTEE OF REVISION 1900-1910.



Scoville	Good	Diehl	Saltler	Hare	Sayre	Gregory	Stevens	Kreners	Hallberg	A. R. L. Dohme
L. Dohme	Squibb	Caspari	Payne	Remington	Lyons	Coblentz	Marshall	Haines	Kraener	
	Lengfeld	Davis	Wilcox	Wall	C. E. Dohme	Melssner	Simmons	Whelpley	Beal	



# THE AMERICAN JOURNAL OF PHARMACY

JUNE, 1910

## SUGGESTED U.S.P. TESTS FOR GLYCERIN.

By THOMAS M. STARKIE, Manager, William F. Jobbins, Incorporated.

The Food and Drugs Act having adopted the Pharmacopœia as the standard by which manufacturers must be governed, it is desirable and necessary that the Pharmacopœia requirements should specify such definite, fixed limits of impurities, and tests for determination thereof, as will avoid the possibility of contention between pharmacists and chemists, and in the commercial world, and the attention of the members of the Committee of Revision, meeting in Washington this month, is invited to the subject of Glycerin.

Many of the tests set forth in the Pharmacopœia, official at the present time, are indefinite and unreliable, and allow of so much possibility of contention, particularly by some pedantic analyst, that any glycerin could be claimed as failing to meet the requirements of the Pharmacopœia. It has been contended that in a general way the tests as given in the present Pharmacopœia will, in the hands of an intelligent analyst, enable him to distinguish between a pure and an impure glycerin. Experience over a great many years in the glycerin business has shown that even the most intelligent and careful analysts will differ regarding the Pharmacopœia tests for glycerin.

Tests involving mixing with concentrated sulphuric acid, and heating glycerin with sulphuric acid and alcohol, should be abandoned, inasmuch as they lead to varying results in different hands, and even when carried out with the greatest care may lead to wrong conclusions, and, also, such tests show no more than can

be determined with greater definiteness from tests exactly stated. Tests involving treating glycerin with ammonia and silver salts, or with ammoniacal silver salts, and requiring heating with alkaline copper solutions, are unreliable, and likely to give erratic results in the hands of different analysts, and should be abandoned. Such requirements should obtain that will insure a quality of glycerin with only innocuous limits of impurities, and such as is contemplated by the Food and Drugs Act, and the necessary tests for the determination of the purity of glycerin should be set forth in such language that there can be no erroneous conclusions, regardless of the measure of intelligence of the analyst, conceding always, of course, that the analyst must necessarily have such knowledge and ability in chemistry to make the tests. The requirements also should be such as will avoid any possibility of advantage to any dishonest refiner, by reason of tests that permit of any controversy or contention as to the meaning thereof.

With such purpose in view it is suggested that taste and odor tests be eliminated, since two different individuals' senses of taste or smell are almost invariably widely different, one chemist sometimes being of the opinion that there is a foreign taste or smell, while another equally careful and exacting chemist can detect neither, resulting in contention.

Specifications are herewith submitted as requirements covering all possible impurities to be found in chemically pure glycerin:

*Specific gravity*, not less than 1.249 at 25° C. (=95 per cent. glycerin). Factor of .00061 to be added for each degree of temperature below 25° C., between 15° and 25° C., at which gravity is determined. The gravity to be ascertained by picnometer, or by means of an accurate plummet (as employed with a Westphal specific gravity balance), suspended from the arm of an analytical balance sensitive to one-tenth milligramme.

*Carbonaceous residue*, including mineral and carbonized organic impurities, not to exceed .01 per cent. Test: weigh 50 grammes of glycerin in a tared platinum dish, heat cautiously until it inflames upon direct application of fire (say from lighted match), then remove the source of heat (preferably Bunsen burner), and allow the glycerin to burn away in a place free from draught; transfer the dish to a desiccator, and weigh when cold.

*Ash*, including chlorides, not to exceed .007 per cent. Test: incinerate the carbonaceous residue at a dull red heat until carbon

is entirely burned off; then transfer to a desiccator, and weigh when cold.

*Chlorides*, not to exceed .001 per cent., figured as NaCl. Test: put the ash in 100 c.c. distilled water, add 2 or 3 drops of a cold, saturated solution of neutral chromate of potassium ( $K_2CrO_4$ ) as indicator; then run in, from accurately calibrated burette, N/100 silver nitrate volumetric solution till tinge of permanent red color appears; the c.c. of N/100 silver nitrate volumetric solution used, multiplied by .0005806 for each c.c., and then by 2, giving the percentage of chlorine as sodium chloride.

*Total acid equivalent*, in terms of NaOH, not to exceed .02 per cent. Test: weigh 100 grammes of the glycerin, and dissolve in 100 c.c. of distilled water. Use phenolphthalein solution as indicator. Run in 10 c.c. of N/10 NaOH solution (3.976 grammes of NaOH to 1 litre) from a burette, heat to boiling over Bunsen burner, and continue boiling for three or four minutes, then titrate with N/10  $H_2SO_4$  solution (4.8675 grammes per litre) run in from a burette, until pink color just disappears. The NaOH solution used, less the  $H_2SO_4$  solution used, must not exceed 6 c.c. to neutralize.

*Arsenic* not to exceed 1 part in 100,000; to be determined by the Gutzeit test, and 5 c.c. of a 1-in-10 aqueous solution of the glycerin placed in a narrow-necked flask with 2 grammes of zinc, 20 c.c. of hydrochloric acid (22.5 c.c. concentrated and 77.5 c.c. water). The flask is closed by a filter paper saturated with alcoholic solution of mercuric chloride, and dried. The neck of the flask contains a roll of cheese cloth impregnated with 10 per cent. lead acetate, to prevent any hydrogen sulphide from reaching the sensitive paper. The flask, 60-75 c.c., should have a narrow neck, and the circle of paper exposed should be about 1 cm. in diameter. The action is allowed to continue until the greater part of the zinc is dissolved, and at that time the paper should not be stained a distinct yellow or orange.

*Silver nitrate test*: An aqueous solution (2 c.c. of glycerin to 10 c.c. of distilled water), with 5 c.c. of N/10 silver nitrate solution; the mixture shaken and placed in a dark place for 10 minutes may assume a slight pink or gray tinge, but must not turn red nor black, nor give a precipitate (limit of chlorides and impurities having reducing properties).

Glycerin conforming to the above tests will insure such purity

as is necessary and desirable, and applicable for use in medicines, foods, or drugs, and are requirements which no honest refiner of glycerin can reasonably make objection to.

The question of sugar adulteration was investigated about three years ago by the United States Department of Agriculture, prompted by the assertion that no American glycerin was obtainable that would not reduce Fehling's solution. The investigation led to finding that the glycerin of reputable American refiners did not reduce Fehling's solution. Sugar adulteration of glycerin, however, has long since ceased to be practised, and the test with Fehling's solution is no longer employed, as sugar, if present, would increase the carbonaceous residue, and is, therefore, covered by the definite, fixed limits of carbonaceous residue in the proposed requirements.

## PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE  
RELATING TO PHARMACY AND MATERIA MEDICA.

BY M. I. WILBERT, Washington, D. C.

Pharmaceutical history has been materially augmented by the recent happenings, both in this country, as well as abroad, though the observer would be rash, indeed, who would attempt, at this early date, to designate which of the several happenings is destined to have the more far reaching influence on the progress of pharmacy at large.

The annual meeting of the American Pharmaceutical Association, coming, as it did, immediately before the decennial meeting of the U. S. Pharmacopœial Convention, was unusually well attended and the members present appeared to take more than ordinary interest in the program that had been provided for their consideration. The general meetings of the Association as well as all of the sessions of the several sections were well attended, the papers presented were both numerous and meritorious and the discussions were, usually, much more interesting, certainly more comprehensive, than in former years.

Pharmacopœial revision was freely discussed both in and out of meeting and at least several of the features of the meeting, in this connection, were unusually interesting and will undoubtedly



prove to be of value in the coming revision of the Pharmacopœia of the United States.

Among the more interesting features, bearing upon the revision of the Pharmacopœia, were the discussion of the report of the A. Ph. A. Committee on the U.S.P. in the Section on Scientific papers and the symposium on foreign pharmacopœias in the Section on Practical Pharmacy and Dispensing.

These two events will probably be recognized by those present as being the more interesting, certainly the more influential, events of the week and it is unfortunate indeed that it will be impossible to reflect, in the printed report of the proceedings, the spirit and the earnestness manifested by those taking an active part in the discussion.

The United States Pharmacopœial Convention, held in Washington, May 10, 11, and 12, 1910, will undoubtedly be recorded in history as the beginning of a new era in matters pharmacopœial though the ultimate outcome, at the present time, is quite problematical.

It is perhaps unfortunate that the general medical practitioner and the teachers of clinical medicine and applied therapeutics in medical schools are not more liberally represented on the General Committee of Revision, though on the other hand it is a matter for congratulation to note that the new thought in pharmacal therapy, as represented by experimental pharmacology, is well represented; no less than six members of the General Committee of Revision being directly interested in this line of work.

Altogether it is fair to assert that the General Committee of Revision, despite the hit or miss fashion in which it was necessarily selected, is unusually well balanced and is fully representative of the interest manifested by the members or delegates present.

Forecasting the possible outcome of the present revision an article on the U.S.P. (*Drug. Circ.*, 1910, w. 54, p. 224) concludes:

"It would appear that we have once more come to the parting of the ways, and that the delegates gathered at the decennial meeting of the United States Pharmacopœial Convention, on May 10th of this year, must decide whether or not the United States Pharmacopœia IX is to reflect the bright light of the morrow or the dim after-glow of the waning day. In other words, they must decide between the acceptance of knowledge, science and truth, or the retention of speculation, empiricism, and self-de-

ception; between a pharmacopœia for the future along the lines laid down by the originators of the American Pharmacopœia, or a book of standards for the thousand and one articles that have been and are being used as medicine without any definite knowledge of how or why. . . . Which will it be, a repetition of the stagnation evidenced in 1870, or of the progress recorded in 1880? The delegates present at the convention will decide, and the people at large will be benefited or injured by their decision to the extent to which it will foster or retard progress in the science of medicine."

An editorial in the *New York Medical Journal* (May 14, 1910, p. 1020) commenting on the Pharmacopœial Convention, says in part:

"The only important difference of opinion which arose in the Convention was regarding the scope of the Pharmacopœia. In discussing the principles laid down by the Convention for the guidance of the Committee of Revision some of the members of the Convention desired to limit the scope of the Pharmacopœia so as to make it available as a text book, while others wished to widen its scope so as to include all medicinal substances in general use, whether of approved therapeutic value or not. While the recommendation to the Committee of Revision was general in character, its purport was in favor of widening of the scope. The Convention took the ground that the extent to which a drug was used was a safer criterion of its availability for introduction into the Pharmacopœia than the expression of expert opinion regarding its therapeutic value. Consequently the use rather than the therapeutic value of a drug will be taken as a guide by the committee regarding admissions and deletions.

"The election of Dr. Harvey W. Wiley, chief of the Bureau of Chemistry of the United States Department of Agriculture, and charged in his official capacity with the enforcement of the Food and Drugs Act, to the presidency of the Convention gives assurance of complete harmony between the Government and the Committee of Revision. The substitution in this office of a chemist and government official for a physician and therapist may be taken as indicative of the change in the status of the Pharmacopœia from that of a purely academic pronouncement to a book of legal standards."

The general principles adopted by the Convention for the guidance of the Committee of Revision are well worthy careful

consideration on the part of those interested in the revision of the Pharmacopœia and to many at least these general principles would appear to leave the responsibility for the scope and content of the Pharmacopœia as well as many of the details of the revision entirely with the Committee of Revision.

One of the more important of these principles, No. 14, refers to publicity and recommends that: The general Committee of Revision be authorized to make public for comment and criticism an abstract of standards and tests before final adoption.

The value of preliminary publication of proposed pharmacopœial standards is well illustrated by the discussion that has been aroused in German and English Pharmaceutical Journals, through the preliminary publication of proposed changes in the German and British Pharmacopœias. In Great Britain the publication of the monographs proposed for the Ph. Brit. V. has been followed by a full and free discussion of the several proposed requirements and the resulting information that has been offered will, no doubt, be of advantage to the editors of this particular portion of the Ph. Brit.

An editorial (*Chem. & Drug.*, Lond., 1910, March 26, p. 64) in discussing the prior publication of the proposed pharmacopœial monograph for essential oils points out that this is the first time that this course has been attempted in connection with the Ph. Brit., and commends the move as being one in the right direction, despite the fact that it still remains to be proved how far the new method will meet the wants of the case. There can be no two opinions about the fact that it is a rational experiment devised for the good of all interested.

*Ph. Germ. V.*—A list of the proposed changes to be made in the German Pharmacopœia is published in the *Pharm. Zeitg.* (1910, v. 55, p. 177). The changes include admissions, deletions, changes in the Latin title, and a number of changes in the requirements for the several articles.

An editorial (*Pharm. Zeitg.*, Berlin, 1910, v. 55, p. 269) commenting on the changes proposed for the new edition of the German Pharmacopœia, points out that the proposed additions include 63 separate titles and 12 general headings. Among these 63 titles are 17 substitute preparations, 2 new oils, and 5 new drugs. The number of articles proposed for deletion amounts to 32, so that the new Pharmacopœia will include in round numbers

40 additional titles. Even with this addition the German Pharmacopœia will contain fewer medicaments than the majority of other foreign pharmacopœias. This is considered as evidence of the scientific development of medicine in Germany.

The following titles proposed for the corresponding trade names will illustrate the difficulties that confront the prospective user of the Ph. Germ. V.:

Paraminobenzoyldiaethylaminoethanolum hydrochloricum.....	Novocaine
Benzoylaethyltrimethylaminopropanolum hydrochloricum.....	Stovaine
Tropacocainum hydrochloricum.....	Tropacocaine
Trimethylbenzoxypiperidinum hydrochloricum.....	B. Eucaïne
Aethylmorphinum hydrochloricum.....	Dionin
Diacetylmorphinum hydrochloricum.....	Heroin
Acidum acetylo-salicylicum.....	Aspirin
Pyrazolonum phenyldimethylicum salicylicum.....	Salipyrine
Pyrazolonum dimethylaminophenyldimethylicum.....	Pyramidon
Natrium Arsanilicum .....	Atoxyl

Some criticism has been aroused in Germany by the proposed use of the full chemical name for the new additions to the German Pharmacopœia. It is proposed, for instance, that in place of the chemical name for novocaine the name aethamin be used, and for stovaine the name propamin (*Pharm. Ztg.*, Berlin, 1910, v. 55, p. 270).

J. Prescher, in a communication to *Pharm. Zentralh.*, 1910, v. 51, p. 288, discusses the nomenclature of the haloid salts of sodium, ammonium, calcium and magnesium in the Ph. Germ., and points out that "chloratum" has been and is likely to continue to be mistaken for the designation frequently used for the "ic" salts of the same elements.

NEW ITALIAN PHARMACOPŒIA.—An editorial (*Chem. & Drug.*, London, 1910, Feb. 26, p. 327) commenting on the new Italian Pharmacopœia, shows that in certain directions tests are adapted to the requirements of the average pharmacist rather than to please the analytical specialist.

SERVIAN PHARMACOPŒIA.—The recently published "Pharmacopœia Serbica, Editio secunda," embodies several interesting innovations. To overcome the criticism that deleted articles are no longer subject to any official requirements it is provided that when an article not official in the second edition but described in the first edition of the Servian Pharmacopœia is prescribed by a



physician the article, as dispensed, must comply with the requirements laid down in the former edition of the Pharmacopœia. The provisions of the Brussels Conference are closely adhered to. Physical and chemical tests have been added. Patented chemicals are introduced and described under their chemical titles (*Pharm. Post*, 1910, v. 43, p. 169).

PHARMACOPŒIAL COMMENTS.—The following abstract from an editorial (*Pharm. J.*, London, 1910, v. 30, p. 510) serves as an illustration of the interest taken abroad in every thing pertaining to pharmacopœial revision:

“As an example of thoroughness in the department to which it specially applies Bulletin No. 58 of the Hygienic Laboratory of the United States is probably unequalled anywhere. . . . Even a casual perusal of this volume will quickly convince the reader that ‘a maximum amount of disinterested information’ has been collocated in a manner which may well serve as an example to older countries. The status of the U.S.P. as the official standard for determining the purity and strength of widely used medicaments could not be maintained on better material than is to be found in this digest, for the compilation of which the pharmaceutical and chemical literature of the whole civilized world has been ransacked in a way which, one is almost compelled to think, can only be done in America. The compilers having hit upon what is undoubtedly the right way to go about it, have apparently left no leaf unturned in their efforts to find material which in any way dealt critically with official articles. . . . International standards are fully considered in twenty-two pages, while the remaining 411 pages are taken up with comments on official articles drawn from all available sources, and which for the most part constitute the material with which the compilers may make or mar their National Pharmacopœia.”

INTERNATIONAL CONGRESS.—The International Pharmaceutical Congress, to be held in Brussels from September 1 to 5, 1910, is attracting considerable attention abroad, particularly in Germany and France.

At a recent meeting of the German Pharmaceutical Society, held in Berlin, the several propositions that have been submitted were discussed at some length. The desirability of greater uniformity in the strength of test solutions and in the method of

using them as directed in the several pharmacopœias was particularly emphasized.

ALKALOIDAL CONTENT OF SOLANACEOUS PLANTS.—T. Chevalier (*Comptes rend*, 1910, v. 150, p. 344) points out that the generally accepted statement that wild belladonna is richer in total alkaloid than the cultivated plant would appear to require modification. A series of cultural experiments show that by employing the right manure the proportion of alkaloids in the leaves of solanaceous plants may be more than doubled.

APOMORPHINE HYDROCHLORIDE.—An abstract from articles by E. Harnack, H. Hildebrandt and others shows that a trade preparation sold as apomorphine hydrochloride contained from 66 to 75 per cent. of trimorphine hydrochloride, which has a different physiological action to apomorphine. It is generally known that apomorphine and trimorphine hydrochloride cannot be sharply separated by salting out with hydrochloric acid. The presence of large quantities of trimorphine hydrochloride, however, is thought to be objectionable (*The Pharm. J. and Pharmacist*, London, 1910, 545).

BORIC ACID, AS A FOOD PRESERVATIVE.—The conclusions which Dr. Julius Bernstein, bacteriologist to the City of Westminster, draws from a series of experiments directed to find out the effect of boric acid on foods are worthy of attention. He finds that boric acid to the extent of 20 grains to the pound prevents objective decomposition, such as is detectable by smell. If objective putrefaction has commenced, it inhibits further changes of this kind, possibly leading to diminution in the smell. It has a marked selective activity on the various organisms, inhibiting the growth of yeasts and organisms of the *proteus* group, and possibly other harmless saprophytes, though not the organisms of the *coli* group. (*The Pharm. J. and Pharmacist*, London, 1910, p. 509).

BUCHU LEAVES.—A correspondent discusses the collection and marketing of buchu leaves in Cape Colony and points out that the genus *Barosma* is peculiar to the Cape, as many as eight varieties having been classified. Of these, 3 are considered of medicinal value in Europe, although in Cape Colony many other varieties are used in domestic medicine. *Barosma betulina*, the official variety, is the one chiefly collected, as it commands much higher prices, as does *B. serratifolia*. In this connection it is interesting to note that 20 years ago the value of these two

varieties was reversed. The correspondent also points out that the buchu market in London mainly depends on the American demand (*Chem. & Drug.*, London, 1910, March 5, p. 338).

COTO BARK.—An editorial in the British *Pharmaceutical Journal*, 1910, v. 30, p. 231, asserts that true coto bark has long been unobtainable in commerce, and it is generally understood that the article now in use is paracoto bark, which possesses similar properties, though not yielding identical chemical products. But even the paracoto bark has recently become scarce, and there are at present two false barks in commerce, which differ essentially from the genuine coto.

CINCHONA ASSAY.—Bernard F. Howard, commenting on a recent paper by Engelhardt and Jones who assert that "in most of the cinchona barks the relation of the percentages of the four principle alkaloids of the drug is almost constant," expresses the belief that there is an immense variation in the proportions of the four common alkaloids in different samples of cinchona bark. This is, perhaps, best illustrated by the fact that a considerable number of well known Dutch analysts in Amsterdam publish about once a month an official list of analyses of samples of bark up for sale, and a study of these analyses will show at once not only a great variation in the percentage of total alkaloids in various samples of barks but also great differences in the proportion of quinine present to cinchonidine, cinchonine, and quinidine (*The Pharm. J.*, London, 1910, p. 504).

COD LIVER OIL.—An editorial discusses the economic conditions prevailing in the cod liver oil market and points out that the price of Norwegian cod-liver oil has appreciated more than 25 per cent., as Lofoten fishing has proved very irregular, and although the number of fish caught was quite up to the figures of the previous year, the production of medicinal cod-liver oil is 3,756 barrels or 4,357 hectolitres less. The general opinion in Norway is that the livers will be leaner next season (*Chem. & Drug.*, London, 1910, March 26, p. 62).

ERGOT.—An abstract from an article by A. T. Livingstone (*Med. Rec.*, Jan. 29, 1910, through *B. J. M.*) points out that the peculiar province of ergot is to stimulate diseased rather than normal unstripped muscle. However contrary to previous knowledge of ergot, it is practically true that it acts on the diseased organs better than on normal ones containing unstripped muscle fibres. The author

has never found any bad effects from the use of large doses of ergot. He prefers the less refined preparations, since some principle seems to be removed by standardization (*The Pharm. J. and Pharmacist*, London, 1910, p. 496).

MUCILAGE OF ACACIA.—A correspondent calls attention to the need for preserving mucilage of acacia and asserts that the addition of 10 per cent. of alcohol will serve as an efficient and unobjectionable preservative (*Pharm. Ztg.*, Berlin, 1910, v. 55, p. 232).

NUX VOMICA.—Planchon and Tuillet (*Répert. Pharm.*, 1910, v. 22, p. 97) discuss the identity of "Corozo" which has frequently been found as an adulterant of powdered nux vomica. They point out that large and increasing quantities of so-called Australian corozo are now imported into Hamburg.

OPIUM.—Frank Browne discusses the nature and composition of the several varieties of opium and the methods of consuming the drug and its several preparations (*Pharm. J.*, London, 1910, v. 30, pp. 452-453).

THE SUSCEPTIBILITY OF CHILDREN TO OPIUM.—A recent editorial, in the *British Pharmaceutical Journal*, 1910, v. 30, p. 230, discusses the general belief that children are more susceptible than adults to the toxic effects of opium; it is pointed out that children respond as readily as adults to the therapeutic action of opium, and are really less susceptible to its toxic effects.

STERILIZING AMPOULES.—Baroni considers that steam at 112° C. is indispensable for effective sterilization of ampoules. In the case of adrenalin chloride and eserine salicylate a tint sometimes develops owing to the presence of an air-space in the ampoule. This has been obviated by filling the space with a harmless gas, such as carbon dioxide, but the apparatus required is somewhat more complicated than is needed for filling ampoules in the ordinary way (*Chem. & Drug.*, London, 1910, March 26, p. 68).

STANDARDS FOR BRANDY, WHISKY, AND RUM.—Regulations that have been made by the Governor-in-Council and published in the *Hong Kong Government Gazette*, providing standards for brandy, whisky, and spirit, define brandy as a spirituous liquid distilled from the wine of grapes, and "Cognac" as brandy made in the Cognac region from grapes grown therein. Whisky is defined as a spirit obtained by distillation from a mash of cereal grains saccharified by diastase of malt. Rum is defined as a spirit distilled direct



from sugar-cane products in sugar-cane growing countries (*Pharm. J.*, London, 1910, v. 30, p. 422).

**TINCTURE OF IODINE.**—C. Courtot (*Journ. de Pharm. et de Chim.*, 1010, Nr. 67) presents a study of the changes that take place in tincture of iodine and concludes that the products formed are hydriodic acid, acetaldehyde and acetic ether. The reactions taking place he outlines as follows: Through the action of iodine on alcohol hydriodic acid and acetaldehyde are produced; the latter is decomposed by iodine in the presence of water to acetic acid, which, reacting on the alcohol, produces acetic ether (*Pharm. Ztg.*, Berlin, 1910, v. 55, p. 346).

**VOLATILE OILS.**—Hill and Umney present a number of monographs for volatile oils which it is proposed to submit for inclusion in the coming edition of the British Pharmacopœia (*Pharm. J.*, London, 1910, v. 30, pp. 177-181).

*The Chemist and Druggist* (1910, March 12, pp. 94-96) presents a comprehensive comparative table of data on essential oils as propounded by different authors, British Pharmacopœia, Squire's Companion, Hill and Umney, Parry's Essential Oils, and others, the object being to show at a glance the points upon which there is agreement and disagreement.

**AMENYL.**—Amenyl is the hydrochloride of methylhydrostimide and occurs as yellowish needle shaped crystals melting at 227° C., and readily soluble in warm water (*Pharm. Post*, 1910, v. 43, p. 293).

**ARYLARSONATES.**—J. Ernest Lane calls renewed attention to the possible untoward effect resulting from the use of such preparations as atoxyl, orsudan, and soamin. He reports a case of optic atrophy and complete blindness following the use of orsudan in a case of syphilis. Also calls attention to three cases, which recently came under his notice, in which blindness was caused by soamin (*Brit. Med. Journ.*, 1910, v. I, p. 599).

**THE DANGERS OF ORSUDAN AND SOAMIN.**—An editorial in the *Pharmaceutical Journal*, 1910, v. 30, p. 387, calls attention to the numerous reports that have been published recently on the possible dangers that might accrue from the use of orsudan and soamin.

**CETHAL.**—Cethal is cinnamylmethyl with 10 per cent. of thymol. Used for the treatment of pulmonary affections; to be inhaled by means of a special apparatus (*Chem. & Drug.*, London, April 2, 1910, p. 44.)

NEOPYRIN.—Neopyrin is valeryl-amido antipyrine and occurs as white nearly odorless crystals that are but slightly soluble in water. The substance melts at  $103^{\circ}$  C. and has a bitter, quinine-like taste. On boiling with alkali or dilute acid neopyrin is split into amidoantipyrine and isovalerianic acid (*Pharm. Post*, 1910, v. 43, p. 293).

PHENOL, ANTIDOTAL EFFECTS OF ALCOHOL UPON.—Novack (*Monthly Ency. and Med. Bull.*, Aug., 1909, v. 42, p. 1132) presents the following conclusions drawn from an investigation on the antidotal effects of alcohol upon phenol: (1) The peculiar phenomena by reason of which alcohol has been acclaimed an antidote to phenol are the result of its solvent and repellent properties and not of any chemical antagonism. (2) Phenol, or carbolic acid, although it is a powerful corrosive, limits its destructive progress by the formation of an albuminous coagulum. (3) Alcohol is of great value externally when used early, but when used late the destruction of tissue is not prevented, although the appearance is better. (4) On account of the repellent and solvent properties of alcohol it is dangerous to be left in the stomach together with the phenol. (5) The advised treatment is first lavage with some solution as the magnesium-sulphate-albumin mixture, followed by lavage with a solution of alcohol as a clearing agent (*Pharm. J.*, London, 1910, v. 30, p. 268).

PROTARGOL.—F. Goldmann, in discussing the dispensing of protargol, warns against the use of glycerin to facilitate solution and asserts that glycerin is not only objectionable but also unnecessary. He points out that an aqueous solution of protargol can readily be prepared by sprinkling the substance on the surface of the distilled water and allowing to stand for a few moments. He concludes that solutions of protargol should be freshly prepared, should contain no glycerin and should not be prepared by the aid of heat (*Apoth. Ztg.*, Berlin, 1910, v. 25, p. 274).

## U. S. PHARMACOPŒIAL CONVENTION OF 1910.

The ninth decennial U. S. Pharmacopœial Convention convened on the morning of May 10 in the large auditorium of the New Willard Hotel, Washington, D. C. It was a gathering representative of the varied interests in the professions of medicine and pharmacy and the drug trade as well.

The Convention was called to order by Prof. Otto A. Wall, the Second Vice-President, upon whom devolved the duties as presiding officer owing to the illness of the President, Dr. H. C. Wood, and the death of the First Vice-President, Prof. A. B. Prescott.

Nearly every one present recognized that the deliberations of the few days furnished an opportunity for the expression of opinions, which would not recur again for ten years. Delegates and alternates representing 158 institutions—80 medical and 78 pharmaceutical and chemical organizations—were in attendance. The total number of 311 accredited delegates, included 140 medical and 171 pharmaceutical and chemical representatives. While there may be some question as to the limit and scope of the U. S. Pharmacopœia it is quite certain that the principle of general use of an article will not be the sole criterion for its admission. The last ten years have seen the recognition of a principle that is surely in the direction of progress. Ten years ago the President of the Convention stated that "if powdered brickdust was employed by the medical profession then it should be admitted into the Pharmacopœia." At the Convention of 1910 the principle was discussed that not only must a substance be in general use, but that it must also have some value as a remedial agent in order to be admitted into the Pharmacopœia. After having been acceded to by a good majority this principle was subsequently, on motion of Dr. Solis Cohen and without any additional discussion, eliminated and we believe that this was due to a misunderstanding of the purport of the recommendation from the outgoing Committee of Revision.

The address of welcome by Secretary Charles Nagel of the Department of Commerce and Labor was appropriate and indirectly suggestive of the motive and spirit which should dominate the deliberations of a convention which concerns the protection of the

public health. He said that there must be co-operation of the representatives of industry, commerce and government; that the delegates were assembled to consult and confer in order that they might develop their professional work; and that in the elevation of standards which are intended for the protection of the public health and which are to be adopted by the Government, it is desirable that this be done in such a manner that commerce is not interfered with and no new regulations are required for their enforcement.

The address of His Excellency Senor Calvo, the minister to the United States from Costa Rica was suggestive of the opportunity afforded the convention to make the U. S. P. an American Pharmacopœia. He stated that the Spanish American population amounted to 40,000,000 people. He also referred to the fact that the U. S. Pharmacopœia is one of the recognized pharmacopœias official in Costa Rica and in several of the States of South America.

The address of President Wood was then read by Dr. Wall. It was in printed form and copies were distributed to the delegates. As the address was being read no doubt those who had intimately known Dr. Wood and were present at the 1900 Convention thought of him and saw him as he was then, the ablest exponent of the medical profession and as the leader and most magnetic personality of that convention. The present address revealed the character that has been shown in all of the papers of Dr. Wood during the past fifty years and is a fitting close to a life of over-strenuous labor in the interest of the professions of medicine and pharmacy, he being as well known to the pharmacists of the United States, and indeed throughout the world, as he is to the medical profession.

From the address the following paragraphs are selected as having a bearing on the future work of revision:

The position of the Convention is so anomalous that a parallel is very difficult to find, but the lighting and buoying of the English coast is under the control of a Corporation which is analogous to the U. S. Pharmacopœial Convention in that it exercises legal governmental authority although an independent body. Its power to erect and take charge of the light-houses and beacons of the coast of England was given to it by Queen Elizabeth in 1573, and its work has been so satisfactory that whilst the coasts of Scotland and Ireland are under government care, the Brothers of the Trinity still remain masters of the English coast.

As it was with the Corporation of Trinity House, so originated in



the early days of the American Republic, not by law but by voluntary action and consent, the Convention of the U. S. Pharmacopœia; but to-day, incorporated and its actions legalized, it constitutes the power which regulates the relations between the professions of pharmacy and medicine, and gives the standard of legal purity for certain substances used widely for other than medical intent.

The Corporation of Trinity House has maintained its supremacy and the character of its work by its conservatism, and by its refusal to widen the circle of the Executive or the character of its membership. As with it so do I believe that the U. S. Pharmacopœial Convention will, to the great benefit of the professions of pharmacy and medicine and of the people of the United States, maintain its own existence by conservatism, by guarding well the portal of entrance to the Convention, and by making scientific and practical fitness rather than geographic representation the requirements for membership, especially in its Executive.

President Wood also referred to the fact that as the Spanish translation of the U. S. Pharmacopœia had become the official Pharmacopœia of Cuba, he believed that the University of Havana should be given the inherent right to send a delegate or delegates to the Convention, because to the University of Havana we ought to look for the translation of the Pharmacopœia into the Spanish language. This recommendation was subsequently approved by the Convention. During the reading of the address there was present upon the platform Dr. José Guillermo Diaz, of the University of Havana, who translated the U. S. Pharmacopœia into Spanish and to whom in large part is due the popularization of the Spanish edition. Dr. Diaz was later introduced to the Convention and he and his colleagues Dr. Juan Guiteras and Dr. José Alacan also Professors in the University of Havana were extended the privileges of the floor.

One other matter might be mentioned which was considered by President Wood in his address. He says:

In 1902, your President and Dr. Frederick B. Power, Ph.D., an American chemist, Director of the Wellcome Chemical Research Laboratories of London, were appointed by the Secretary of the Interior as delegates to represent the U. S. Government in the International Conference for the Unification of the Formulæ of Heroic Medicines, which had been called by the Belgian Government and which met in Brussels in September, 1902. Although attempts had been made before to obtain such unification, and failed, this Conference fully achieved the object for which it was summoned, namely—the making of a list of drugs which were considered actively remedial and yet capable of doing great harm, with a list of preparations and their strength; so that the traveller can, when the work of the Conference has been accepted by the various nations individually, have a

prescription compounded of the same strength in any city of a Nation party to the Conference. The Committee on Revision of the U. S. Pharmacopœial Convention has in great measure conformed to the recommendation of the meeting at Brussels. The failure to do so completely seems to me the one blot on their work.

Nov. 11th, 1908, I received from the Acting Secretary of State a translation copy of a letter from the Belgian Legation concerning the creation of a permanent institution, to be called the International Secretariate for the Unification of Pharmacopœias, located at Brussels, its expenses to be paid by annual quotas from the adhering nations. In reply, I wrote to the Hon. Robert Bacon that such a Secretariate seemed to me so foreign to the immediate objects of the U. S. Pharmacopœial Convention, and so open to the possibilities of serious pecuniary responsibilities, that I personally could not endorse it, but would refer the matter to the U. S. Pharmacopœial Convention of 1910. I have heard nothing further concerning this subject, and have transferred all my correspondence to Dr. Murray G. Motter, Secretary of the U. S. Pharmacopœial Convention. With this information I leave this subject to be decided as may be thought fit by you.

The address of Professor Joseph P. Remington, Chairman of the Revision Committee was devoted in large part to a summary of the results achieved and the trend of events during the past ten years. He pointed out the grave responsibilities connected with the work of the next revision of the Pharmacopœia and stated that the Committee would receive greater aid from manufacturers and importers than heretofore and that the next Committee would be embarrassed with riches rather than a lack of information and that the greatest difficulty will be to make a wise selection for the U. S. P. IX. He also referred to the fact that the health and well-being of the nation depends in a large measure upon the work of the Convention and that if the Committee of Revision fails to recognize the responsibilities of the situation the sceptre must pass from the hands of the Convention forever.

It was fitting that the Chairman of the Revision Committee should give due credit to Professor Diaz for his services in the Spanish translation of the U. S. Pharmacopœia and also to Surgeon-General, Dr. Walter Wyman for his co-operation in fixing the standards for Diphtheria Antitoxin and especially in the preparation of the "Digest of Comments" on the Eighth Decennial Revision.

Professor Remington as Chairman of the Committee of Re-

vision also presented in printed form the general principles to be followed in revising the U. S. Pharmacopœia IX. As these principles had been formulated by the members of the outgoing Committee of Revision they received the endorsement of the Convention, though not without some discussion. As we have not sufficient space to print all of the general principles accepted it may suffice to call attention to some of the more important of them.

**SCOPE OF THE PHARMACOPŒIA.**—We recommend that the Committee of Revision be authorized to admit into the Pharmacopœia any medicinal substance of known origin; but no substance or combination of substances shall be introduced if the composition or mode of manufacture thereof be kept secret, or if it be controlled by unlimited proprietary or patent rights. Substances used only for technical purposes should not be admitted to the next Pharmacopœia, and a statement should be placed in the preface to the effect that standards of purity and strength, prescribed in the text of the Pharmacopœia, are intended solely to apply to substances which are used for medicinal purposes or in determining the purity and identity of the same.

**SYNONYMS.**—We recommend that the list of synonyms should be enlarged for the next revision, and the synonyms printed in the text of the Pharmacopœia, immediately after the English name of the substance. A statement should be made in the preface of the Pharmacopœia, that substances labeled with synonym, must comply with the same standards, tests and requirements as are demanded for the official article under any name.

**PURITY AND STRENGTH OF PHARMACOPŒIAL ARTICLES.**—We recommend that the Committee be instructed to revise as carefully as possible the limits of purity and strength of the pharmacopœial chemicals and preparations for which limiting tests are or may be given. While no concession should be made towards a diminution of medicinal value, allowance should be made for unavoidable, innocuous impurities or variations due to the particular source or mode of preparation, or to the keeping qualities of the several articles.

The "Purity Rubric," which limits the percentage of innocuous impurities, as introduced into the Eighth Revision, should be continued, and tests and requirements should be appended to each article carrying a "Purity Rubric."

In the case of crude drugs and natural products, the limits of admissible impurities should be placed at such a figure as to exclude any that would not be accepted by other countries.

**INTERNATIONAL STANDARDS.**—The International Conference for the Unification of Formulas for Potent Remedies performed a signal service for all countries by recommending the various pharmacopœias of the world to adopt certain standards for potent medicines. It is recommended that the next Committee of Revision adopt these standards, but it is believed that

it would be unwise to require the acceptance of the details of pharmaceutical or other processes recommended by the International Conference.

If the finished product conforms to the International standards we believe that each Country should be left free to adopt such detail and manipulation as may seem to them best. Nothing should prevent, however, the adoption of the recommendation of the conference, as to details, if in the opinion of the next Committee of Revision, by so doing, the Pharmacopœia can be improved.

**GENERAL FORMULÆ.**—It is recommended that general formulæ be introduced as far as the particular nature of the several drugs will permit, for fluid extracts, tinctures and such other preparations as are made by identical processes, and that the general formula to be followed in each case be merely indicated by reference.

**APPENDING A LIST OF PREPARATIONS IN WHICH AN OFFICIAL ARTICLE IS USED.**—It is recommended that, especially for the convenience of practising physicians, there should be appended after each article in the text a list of the official preparations in which it is used.

A few exceptions may be made to this in such cases as water, alcohol, glycerin, sugar, etc.

**ALCOHOLIC PERCENTAGE IN OFFICIAL PREPARATIONS.**—It is recommended that a range of volume content, of absolute alcohol, be stated in the Pharmacopœia, for each preparation containing alcohol.

**ASSAY PROCESSES.**—We recommend that the Committee be instructed to introduce assay processes for as many of the potent drugs and preparations made therefrom as may be found practicable, provided that the processes of assay are reasonably simple (both as to methods and apparatus required) and lead to fairly uniform results in different hands. As regards the products of such assays, tests of identity and purity should be added wherever feasible.

It is recommended that biological tests or assays, when accurate and reliable, may be admitted.

**COMPOSITE PREPARATIONS.**—It is recommended that new composite (compound) preparations be discouraged as far as possible.

**PHARMACOGNOSTICAL DESCRIPTIONS.**—It is recommended that, with the description of a crude drug, there be included brief, pharmacognostical descriptions, both macroscopic and microscopic where practicable, and there should be added a statement of the appearance of the structural elements in the powder, when examined microscopically, as a means of detecting adulteration.

**POWDERED DRUGS.**—It is recommended that, in the next Pharmacopœia, powdered drugs be required to represent the entire drug unless specifically stated otherwise. Where the drug can be powdered without residue this should be required; in other cases the amount of allowable tailings, gruffs, or residue should be determined and inserted in the text.

**DIAGNOSTICAL REAGENTS.**—It is recommended that there be included in the next Pharmacopœia, such reagents, with standards for strength and purity, as are needed for the proper execution of tests that are valuable and important in the making of a correct diagnosis.



**PUBLICITY.**—In the course of the discussion of the report of the Committee of Revision the following principle was introduced by Dr. W. J. Schieffelin and received the support of the Convention: "It is recommended that the General Committee of Revision make public for comment and criticism an abstract of the changes in descriptions and standards which may be proposed before the final adoption of the report and publication of the Pharmacopœia."

With the exception of the subject of diagnostical reagents all of the principles adopted had received the thorough consideration of the members of the professions interested. As to whether diagnostical reagents should be included in a Pharmacopœia the future only can determine.

On the recommendation of the Board of Trustees the following amendments to the Constitution and By-Laws were adopted after some discussion by the Convention.

I.—Amendment of Section 2, Article II, relating to membership, by inserting after the title "the Surgeon-General of the United States Marine-Hospital Service," the following: "the Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Association of State and National Food and Dairy Departments, the National Wholesale Druggists' Association and the National Dental Association."

II.—Also amendment of Article IV, concerning "Committees and Trustees," by changing the title "Committee of Revision," to that of "General Committee of Revision."

III.—Also Chapter V of the General Committee of Revision was amended so that the general effect was to increase the number of members on the Committee of Revision hereafter to be known as the "General Committee of Revision" from twenty-five to fifty, said General Committee of Revision to create from its own membership an Executive Committee of Revision of fifteen members, to have immediate charge of the work of revision, and also giving to said General Committee of Revision certain advisory and supervisory powers over the work of the Executive Committee of Revision.

Prof. Wm. C. Anderson offered an amendment to include the National Association of Retail Druggists among the associations entitled to representation. This was ruled out of order by the Chairman, Dr. Wall, and was subsequently laid upon the table upon motion of Dr. McCormack. It should be stated that this

amendment could not be acted upon by the Convention as it required a previous recommendation from the Board of Trustees (see this JOURNAL, 1909, p. 524). In some quarters the impression is that Dr. Simmons, of the Board of Trustees, is largely responsible for the Board's failing to recommend the seating of the N. A. R. D. It would be indeed interesting to know just what the minutes of the Board of Trustees show in this connection.

The fact that it was necessary for the Board of Trustees to borrow \$7000.00 during 1902-1905 caused some discussion as to the devising of ways and means not only to relieve this situation, but to provide sufficient funds to carry on the work of revision. A recommendation was submitted by the Board of Trustees, to whom the matter was brought for consideration, that each organization entitled to representation pay a sum of \$50.00 and that failing to comply with this within one year the sum of \$75.00 be required of them; and furthermore, that all new organizations be required to pay \$100.00 on being admitted to the Convention. It was also intended that all organizations which comply with this requirement be allowed 10 copies of the U. S. P. IX. These several recommendations were voted down, it being the unanimous opinion that the Board of Trustees should secure sufficient revenues by increasing the price on each copy of the Pharmacopœia and guarding the copyright. Ten years ago (see U. S. P. VIII, p. xxvi) the balance turned over to the Convention of 1900 amounted to about \$12,000.00. The Convention of 1900 voted an honorarium of \$200.00 to each member of the Committee of Revision so that the balance in the hands of the Board of Trustees during 1900-1901 amounted to nearly \$6000.00. The income from the sales of the VII edition of the U. S. P. during the years 1900-1905 amounted to about \$10,500.00 while the receipts from sales of the VIII edition of the U. S. P. between 1905-1910 amounted to \$87,244.56; and the receipts from the Spanish translation were \$2,762.22. The balance reported by the Treasurer, Dr. G. Wythe Cook, to the Convention of 1910 amounted to \$8,394.01.

The amount expended for publication was \$39,985.42. The Chairman of the Revision Committee received an honorarium of \$5000. The following members of the Committee received an honorarium of \$1000.00 each: Messrs. Coblenz, Dohme, Sadtler and Lyons. The following members received \$600.00 each: Messrs. Caspari, Jr., Diehl, Hallberg, Kraemer and Squibb. The follow-

ing members received \$400.00 each: Messrs. Haines, Kremers, Rusby, Scoville and Stevens. The following members received \$200.00 each: Abel, Davis, Good, Gregory, Hare, Marshall, Oldberg, Payne, Sayre, Wilcox and Wood. The Treasurer received \$200.00 and the Secretary to the Board of Trustees received \$1500.00. For clerical assistance and general office supplies \$17,255.73 was expended, the greater proportion of which was used by the Chairman of the Committee of Revision in circularizing and distributing reports, etc. For chemicals and other supplies about \$1500.00 was expended and for the use of experts \$5263.25 was expended, of which about \$3000.00 was used by the Committee on Inorganic Chemicals. For the Spanish translation \$1500.00 was given to Professor Diaz and the sum of \$1000.00 was paid the Rice Estate. Messrs. Matos and Pablo were awarded \$250.00 and \$97.56 respectively for reading proof of the Spanish translation. In addition to this the Board of Trustees used for travelling and general expenses the sum of \$7855.33. A number of additional items are given in the Financial Report submitted by the Board of Trustees.

The Nominating Committee of 148 members met at 8 o'clock on the evening of May 10th and concluded its work at 4 A.M. on the morning of the 11th. The following nominations were approved by the Convention:

President, Dr. H. W. Wiley, Washington, D. C.; First Vice-President, Dr. N. S. Davis, Chicago, Ill.; Second Vice-President, Chas. Caspari, Jr., Baltimore, Md.; Third Vice-President, Dr. O. T. Osborne, New Haven, Conn.; Fourth Vice-President, Leo Eliel, South Bend, Ind.; Fifth Vice-President, Dr. W. A. Bastedo, New York, N. Y.; Secretary, Dr. M. G. Motter, Washington, D. C.; Assistant Secretary, Dr. N. P. Barnes, Washington, D. C.; and Treasurer, S. L. Hilton, Washington, D. C. Board of Trustees: J. H. Beal, Scio, Ohio; F. W. Meissner, La Porte, Ind.; W. J. Schieffelin, New York, N. Y.; Dr. G. H. Simmons, Chicago, Ill.; and Dr. H. M. Whelpley, St. Louis, Mo.

#### GENERAL COMMITTEE OF REVISION.

1. REMINGTON, JOSEPH P.,  
Professor of Theory and Practice of Pharmacy, Philadelphia College of Pharmacy.
2. KRAEMER, HENRY,  
Professor of Botany and Pharmacognosy, Philadelphia College of Pharmacy.

3. CASPARI, CHAS., JR.,  
Professor of Theory and Practice of Pharmacy, University of Maryland, Department of Pharmacy.
4. DIEHL, C. LEWIS,  
Professor of Practical Pharmacy, Louisville College of Pharmacy.
5. SCHLOTTERBECK, JULIUS O.,  
Professor of Pharmacognosy and Materia Medica, University of Michigan, Department of Pharmacy.
6. LYONS, ALBERT B.,  
Chemist, Nelson Baker & Company, Detroit, Michigan.
7. WOOD, HORATIO C., JR.,  
Associate Professor of Pharmacology, University of Pennsylvania.
8. OSBORNE, OLIVER T.,  
Professor of Therapeutics and Materia Medica, Yale Medical School.
9. WILBERT, M. I.,  
Assistant Pharmacologist, Hygienic Laboratory, United States Public Health and Marine-Hospital Service.
10. RUSBY, HENRY H.,  
Professor of Botany and Materia Medica, College of Pharmacy of the City of New York.
11. HUNT, REID,  
Chief, Division of Pharmacology, Hygienic Laboratory, United States Public Health and Marine-Hospital Service.
12. DOHME, ALFRED R. L.,  
Chemist, Sharp and Dohme, Baltimore, Md.
13. STEVENS, A. B.,  
Professor of Theory and Practice of Pharmacy, University of Michigan, Department of Pharmacy.
14. BERINGER, GEORGE M.,  
Chemist and Retail Druggist, Camden, N. J.
15. EBERLE, EUGENE G.,  
Dean, Department of Pharmacy, Baylor University, Dallas, Texas.
16. SAYRE, LUCIUS E.,  
Professor of Materia Medica, University of Kansas, School of Pharmacy.
17. KREMERS, EDWARD,  
Director of Chemical Laboratories, University of Wisconsin.
18. PUCKNER, W. A.,  
Director, Chemical Laboratory, American Medical Association, Chicago, Ill.
19. KEBLER, LYMAN F.,  
Chief of Drug Laboratory, Bureau of Chemistry, U. S. Department of Agriculture.
20. HALLBERG, CARL S. N.,  
Professor of Theory and Practice of Pharmacy, University of Illinois, School of Pharmacy.
21. LAWALL, CHARLES H.,  
Associate Professor of Theory and Practice of Pharmacy, Philadelphia College of Pharmacy.



22. ROSENGARTEN, GEORGE D.,  
Chemist, Powers—Weightman—Rosengarten Company, Philadelphia,  
Pa.
23. COBLENTZ, VIRGIL,  
Professor of Chemistry, College of Pharmacy of the City of  
New York.
24. HATCHER, ROBERT A.,  
Professor of Pharmacology, Cornell University, Medical Depart-  
ment, New York.
25. GOOD, JAMES M.,  
Professor of Theory and Practice of Pharmacy, St. Louis College  
of Pharmacy.
26. ARNY, HARRY V.,  
Professor of Theory and Practice of Pharmacy, Cleveland School  
of Pharmacy.
27. KOCH, JULIUS A.,  
Professor of Chemistry, University of Pittsburgh, Department of  
Pharmacy.
28. SADTLER, SAMUEL P.,  
Professor of Chemistry, Philadelphia College of Pharmacy.
29. BODEMANN, WILHELM,  
Retail Druggist, Chicago, Ill.
30. LONG, JOHN H.,  
Professor of Chemistry, Northwestern University Medical School,  
Chicago.
31. RAUBENHEIMER, OTTO,  
Retail Druggist, Brooklyn, N. Y.
32. VANDERKLEED, CHARLES E.,  
Chemist, H. K. Mulford Company, Philadelphia, Pa.
33. SOLLMANN, TORALD,  
Professor of Pharmacy and Materia Medica, Western Reserve  
University, Medical Department.
34. NIXON, CHARLES F.,  
Retail Druggist, Leominster, Mass.
35. ANDERSON, JOHN F.,  
Director, Hygienic Laboratory, U. S. Public Health and Marine-  
Hospital Service.
36. DAVIS, NATHAN S.,  
Professor of Principles and Practice of Medicine and Clinical  
Medicine, Northwestern University Medical School.
37. FRANCIS, JOHN M.,  
Chemist, Parke, Davis and Company, Detroit, Mich.
38. CASPARI, CHARLES E.,  
Professor of Chemistry, St. Louis College of Pharmacy.
39. TRUE, RODNEY H.,  
Physiologist, Bureau of Plant Industry, U. S. Department of Agri-  
culture.

40. GREGORY, WILLIS G.,  
Dean, Buffalo College of Pharmacy.
41. GORDIN, HARRY M.,  
Professor of Chemistry, Northwestern University, Department of  
Pharmacy.
42. ENGLAND, JOSEPH W.,  
Director Scientific Department, Smith, Kline and French Company,  
Philadelphia, Pa.
43. EDMUNDS, CHARLES WALLIS,  
Professor of Therapeutics and Materia Medica, University of  
Michigan, Department of Medicine and Surgery.
44. DIEKMAN, GEORGE C.,  
Professor of Theory and Practice of Pharmacy, College of Pharmacy  
of the City of New York.
45. MARVEL, PHILIP,  
Physician, Atlantic City.
46. BARTLEY, ELIAS H.,  
Professor of Chemistry, Toxicology and Pediatrics, Long Island  
College Hospital, Brooklyn, N. Y.
47. HAINES, WALTER S.,  
Professor of Chemistry, Materia Medica and Toxicology, Rush  
Medical College, Chicago, Ill.
48. ALPERS, WILLIAM C.,  
Retail Druggist, New York.
49. HOPP, LEWIS C.,  
Retail Druggist, Cleveland.
50. PLAUT, ALBERT,  
Wholesale Druggist (Lehn and Fink), New York.

The General Committee on Revision had several meetings on Thursday and Friday and elected the following officers: Chairman, Joseph P. Remington; First Vice-Chairman, C. Lewis Diehl; Second Vice-Chairman, H. C. Wood, Jr.; Secretary, C. H. LaWall.

The Executive Committee will be selected by ballot of the General Committee of Revision which will be effected by correspondence.

A number of written communications were received and a number of recommendations were adopted and referred to the General Committee of Revision. Among these were recommendations from the American Pharmaceutical Association, the Philadelphia Branch of the A. Ph. A., the Philadelphia College of Pharmacy, Section on Dermatology of the American Medical Association, etc. The delegates from the Medical Society of New

Jersey presented the following code of ex cathedra rules formulated by Dr. Henry L. Coit of Newark, N. J. which was referred to the General Committee of Revision and Board of Trustees.

ETHICAL RULES FOR THE GUIDANCE OF PHYSICIANS AND PHARMACISTS IN  
THEIR RELATIONS WITH ONE ANOTHER.

*Propositions.*

FIRST.—Ethical principles or standards of right conduct exist, irrespective of their formulation or codification.

SECOND.—Ethical rules are calculated to elevate standards of moral conduct and to foster a spirit of harmony between professional men.

THIRD.—A code of ethics is designed not only for the restraint of those who are actuated by unworthy motives, but for the guidance of those, also, who seek to be governed in their actions by high and true principles.

*The Duties of the Physician to the Pharmacist.*

FIRST.—The physician has no moral right to discriminate in favor of one pharmacist to the detriment of another, except for dishonesty, incompetency or unscientific methods of work.

SECOND.—The physician is never justified in receiving from a pharmacist gratuities in return for patronage; in depositing secret formulas with an individual pharmacist, or by word or deed to jeopardize his professional reputation.

THIRD.—The physician may sometimes find it an advantage to the patient to dispense the medicine; yet in the main it must be regarded as a subterfuge and a hindrance to all interests involved. The physician should, if practicable avail himself of the superior technical skill of a trained pharmacist in the preparation and dispensing of medicines.

*Duties of the Pharmacist to the Physician.*

FOURTH.—The pharmacist who recommends drugs or medicines for specific remedial purposes either directly or through the avenues of advertisement thereby exceeds the limits of his profession and commits an act unworthy of his calling.

FIFTH.—The pharmacist who consents to diagnose disease or prescribe for patients except where emergencies arise, without a proper medical training, assumes responsibilities for which he is not qualified and justly incurs the disapproval of physicians.

SIXTH.—The pharmacist transgresses his true province when for commercial purposes he issues to physicians printed matter setting forth the therapeutic indications for the use of drugs or medicinal preparations. The constituents of a drug or compound together with its chemical and physical properties should be a sufficient guarantee of its utility.

*The Duties of the Physician and the Pharmacist to the Public.*

SEVENTH.—The combined efforts of the physician and the pharmacist are required to protect the public from the nostrum maker, the pseudo-scientific pharmacist, the sectarian physician and drug vendor, and the two should be in continual alliance to demand the extermination of these commercial and mercenary institutions.

EIGHTH.—The physician and the pharmacist should, as far as possible, limit the multiplication of manufactured proprietary compounds. It must be regarded as reprehensible to encourage the use of these remedies to the exclusion of those which are official in the pharmacopœias. It is also their plain duty to discourage the use and sale of all medicines which lead to baneful drug habits.

NINTH.—The best interests of the patient are undoubtedly conserved by the custom of physicians to practice rational therapeutics to the exclusion of those methods which tend to the use of many remedies or those of unknown composition; and the supreme effort of the dispensing pharmacist should be to complete the circle of therapeutics by supplying the demands of experimental and clinical teaching with eligible and trustworthy preparations.

In accordance with a motion by H. M. Whelpley, the Secretary was instructed, by the Convention, to furnish the pharmaceutical and medical press of the country, with the following resolutions.

By E. G. Eberhardt: Resolved, That this Convention recommend to the National and State Food and Drug Inspectors that they urge the purchase of the U. S. Pharmacopœia by such druggists as they may find to be without them.

By H. G. Beyer: That every physician in this country should be requested, by the various medical associations, that he should keep in his office a Pharmacopœia.

The sessions on Tuesday, and on Wednesday morning were presided over by Dr. Otto A. Wall, who showed himself to be an able parliamentarian and dispatched the work with discretion and justice. While there were a number of attempts made on Wednesday morning by some of the members to have the President-elect, Dr. Wiley, presented to the members at that time, Dr. Wall showed that he proposed to present him at a time which could be characterized as the climax of the strenuous sessions already held and which marked the termination of the old Convention and the beginning of the new. At the right moment he introduced the



members of the General Committee of Revision to the Convention. This was followed by the introduction of the members of the Board of Trustees and subsidiary officers of the Association, for each of whom he had an appropriate word of encomium, and finally the presentation of the President-elect, Dr. Harvey W. Wiley, who was brought to the platform by Dr. Wilcox. Dr. Wall then turned over the gavel and office to Dr. Wiley, saying that he "needed no introduction to this Convention as he was well known to all of the people of the United States." In response to calls for a speech, Dr. Wiley said among other things that the man of science is a patriot and a man of deeds. He not only does his duty but he does it promptly. He promised a prompt beginning of the work of revising the Pharmacopœia and a vigorous prosecution of it and that if the Constitution permits the exercise of authority of the President he will wield it in this direction.

On Wednesday afternoon during the discussion of the "General Principles," Dr. N. S. Davis of Chicago occupied the chair and on Thursday morning Dr. O. T. Osborne acted as presiding officer, both of whom discharged their duties in a creditable manner.

At the conclusion of the Convention on Thursday morning President Wiley occupied the chair, while resolutions of thanks to the out-going officers, to the Committee on Credentials and Arrangements, etc., were passed. About noon he declared the Convention adjourned to meet on the first Tuesday in May, 1920.

It is not too much to say that the Convention just concluded has shown a progressive spirit to a degree that could hardly have been anticipated. Professor Remington, as Chairman of the Committee of Revision, called attention to the fact that there could be but one thought in Pharmacopœia work and that was that "the best and always the best" must be found therein. President Wiley reminded the members of the Committee of Revision that as patriots in the service of their country they must endeavor to accomplish the work before them promptly. The actions of the delegates, including their resolutions, showed again and again that they did not desire to exercise any restraining influence on the Committee of Revision and that whatever the sciences and arts had produced they expected the members to utilize, wherever practicable, in the preparation of a work and standard that is to become the hand-book of the physician and pharmacist in ministering to the needs of the people who are suffering from disease and in ill

health. Finally, it must be said that the promise of the new Decennial Revision is in some measure due to the efforts of the surviving officers and members of the Committee of Revision appointed in 1900, who have labored in part under the inspiration of those who were taken from the ranks by the silent hand of Death, and who have stood by the work through tempest and calm eager that their work might be adapted to the new order of things and acceptable to the Convention. The new Pharmacopœia (U. S. P. IX), without inviting comparison, ought to be, as we believe it will be, a book of the times, suited to the modern demands and practices of medicine and pharmacy in the best sense of the words and at the same time adapted to the legislative requirements of the Government, which supplements the united efforts of physicians and pharmacists in devising approved and acceptable standards for medicines by giving them the weight and authority of legal standards.

H. K.

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## THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The fifty-eighth annual meeting of the American Pharmaceutical Association was held at the Hotel Jefferson in the City of Richmond, May 3rd to 7th.

It was a notable convention not only by reason of the amount of Association work accomplished, but also because it proved to be the forum for the discussion of pharmacopœial matters, so that the members were well prepared to intelligently discuss and vote upon the subjects which were to be brought in a concrete form before the Pharmacopœial Convention the week following. The large number of papers which were presented in the various sections, the interesting reports from the various standing committees, and the important recommendations from the Council, well indicated that the officers of the Association as well as of the several sections were competent, that the members were loyal, and that the Association truly represented the activities of the pharmacists of the United States.

The weather was excellent, the surroundings were inspiring, and enthusiasm with earnestness characterized the entire proceedings from Tuesday morning till Saturday evening.

Owing to restricted space in this JOURNAL this year a much more condensed account of the meeting will be given than heretofore has been the custom, but we hope later to present abstracts, at least, of all the more important papers.

At the opening session the Convention was fortunate in having addresses of welcome by Hon. William H. Mann, the Governor of Virginia, and Hon. D. C. Richardson, the Mayor of Richmond. The addresses were responded to by Messrs. Whelpley and Beal, respectively. Greetings were also extended from delegates of the National Association of Retail Druggists, the National Wholesale Druggists' Association, the United States Public Health and Marine-Hospital Service, the Department of Agriculture, and the American Medical Association.

The address of Dr. H. H. Rusby, the President of the Association, had been previously published in the *Bulletin of the American Pharmaceutical Association* for May (pp. 298-310) and so the members were fully prepared to consider it. It was, as stated by Professor Beal, chairman of the committee, to whom the address was referred, "a frank and fearless treatment of matters which are of vital concern to the Association." Some ten or eleven of the recommendations dealing with methods of increasing the membership, the efficiency of the committees of the Association, and pharmacopœial principles were approved by the Association. A number of the subjects discussed by President Rusby are deserving the further attention of those concerned in the development and coördination of the work of the several bodies that are each striving, more or less independently, to attain the highest degree of usefulness. While the Association was not prepared to consider the desirability and practicability of the publication of the National Formulary by the U. S. Pharmacopœial Convention, there must be sooner or later a closer affiliation between the committees having in charge the N.F. and U.S.P. Again in calling "attention to the great desirability of the imposition of some educational and professional requirements with a corresponding license, for those engaging in commerce in drugs and medicines," President Rusby has presented a problem for the Committee on National Legislation which seems to be of a fundamental nature.

In considering the subject of "danger of commercialization" Dr. Rusby, however, handled a "live wire" which at the present time is a subject for discussion. The Committee on the President's

Address took the position that these opinions should be received by the Association merely as "personal opinions upon questions and policies concerning which reasonable men may justly and honestly differ."

So soon as convenient after the adoption of the Report on the President's Address Mr. C. M. Ford presented the following resolutions which it was moved to lay upon the table, but the motion being lost, were adopted by the Association without any discussion:

*Resolved*, That in the opinion of the American Pharmaceutical Association it is neither wise nor expedient, even in pursuit of schemes which it is claimed will advance the material welfare of dispensing pharmacists, to assail, antagonize, or malign any class inseparably joined to us by commercial or professional ties.

*Further*, That we seriously deprecate the hostile attitude toward the medical profession and the jobbing fraternity of various drug journals assuming to represent pharmacists in general, or some considerable body of pharmacists in particular.

*Further*, That we respectfully urge upon the officers of the American Druggists' Syndicate a more careful supervision of the utterances of their so-called "Organ." Its harsh language is hurtful to pharmacists and embarrassing to them in their relations with one another and with physicians and jobbers.

The mercenary schemes of a few overzealous and adventurous individuals who, being frequently without any training in pharmacy, and who entered its ranks solely for gain and to explain their peculiar ideas of high finance, can have no sympathy with its aims or traditions. Such schemes can be helpful and profitable to only an insignificant few and must necessarily bring inevitable disappointment and disaster to the multitude who follow in their train.

*Be it further resolved*, That we recommend that any movement for the reform of medical practice be allowed to originate and proceed within the medical profession.

*Further*, That we are opposed to any attempt upon the part of the pharmacal press to dictate or compel any such reform, believing as we do that the medical profession is eminently qualified to institute and carry out its own necessary reforms.

The report of the Treasurer, H. M. Whelpley, showed that the total invested funds of the Association, *i.e.*, those on which the interest or only part of the interest can be used amounted to \$28,223.89, being an increase over last year of \$4,680.54. The general secretary, Charles Caspari, Jr., presented a report on the financial accounts in his hand, which related to the receipts



from the sales of the National Formulary and Decennial Index, both reports showing a creditable balance in hand.

The Nominating Committee presented a report giving a list of nominees for the respective offices, which list will be submitted to, and voted upon by, the members through the mails.

The Council recommended that Professor Dr. Arthur Meyer of Marburg, Germany, and Professor Dr. A. Tschirch of Berne, Switzerland, be made Honorary Members, which recommendation was approved by the Association and these eminent pharmacognosists were accordingly elected as honorary members of the Association.

The Committee on Membership reported that during the year 216 new members had been elected. It was also requested that in the future the names of applicants for membership be submitted to their respective State representatives upon the Committee on Membership for approval, before being voted upon by the Council. An application for permission to form a Nashville Branch of the A. Ph. A. was received by the Council and granted. A motion was also passed that the Association have official numbered buttons in lieu of the local badges. The next annual meeting will be held in Boston from August 14th to 18th, 1911 and C. Herbert Packard was selected by the Council as the Local Secretary.

The officers of the Council for the ensuing year are: Chairman, James H. Beal; Vice-Chairman, Henry H. Rusby; and Secretary, Joseph W. England. The following officers of the Association whose election is dependent upon the recommendation of the Council were re-elected: General Secretary, Charles Caspari, Jr.; Treasurer, H. M. Whelpley; Reporter on the Progress of Pharmacy, C. Lewis Diehl; Editor of the *Bulletin*, C. S. N. Hallberg. The Historian, a permanent officer of the Historical Section was made a member of the Council Ex-officio. George M. Beringer was re-elected Chairman of the Committee on Unofficial Standards and the following new members were elected: C. A. Dye (in place of G. B. Kauffmann); and H. H. Rusby (in place of A. I. Cohn).

One of the most important steps taken by the Association was the approval of the proposal to launch the *Journal of the American Pharmaceutical Association*, the first number of which is to appear in 1911. The scope of the *Journal* is to include editorial comments, signed editorials, original articles and abstracts of recent literature relating to pharmacy. It was decided, also, to issue the Report on the Progress of Pharmacy at the end of each fiscal year in the

form of a bound volume. The members of the Association will receive the monthly journal as issued and the bound report at the end of the fiscal year. It is proposed that the size of the reading page of the *Journal* shall be practically equal to that of the present page of the *Proceedings and Bulletin*. The publication of the *Journal* will be under the direction of a Committee on Publication of nine members.

The reports of a number of special committees were presented, including that on Reorganization by C. S. N. Hallberg; and one of the A. M. A. on the National Formulary by Dr. Robert A. Hatcher, etc.

The following is an abstract of the lengthy report of the Committee on National and State Legislation which was read by the Chairman, S. L. Hilton:

The field of legislation in which the A. Ph. A. may become effective and should be interested in, should be referred to one committee that has been carefully selected and well instructed with respect to the wishes of the association as to their attitude on all questions pertaining to national legislation.

The original Coudrey bill providing for the editing and publishing of the U.S.P. should be opposed and defeated. The Coudrey bill providing that all drugs shall be of the standard required by the U.S.P. and N.F. and where no standards are provided granting the power to the Secretary of Agriculture to establish such standards should be carefully considered. The latter proposition providing for the establishing of standards needs no argument, providing that all interests be carefully considered, would be an advance in the right direction and redound to the good of every one.

The first proposition, however should be carefully considered, under the provisions of the Food and Drugs Act, any drug may differ from the standard if it is clearly explicitly stated on the label. By the terms of this provision the field is left open for adulteration and sophistication and the object sought by the Coudrey bill is to overcome this difficulty. The Chairman stated that personally he felt that this provision of the Food and Drugs Act should be amended so that no deviation from the standards should be permitted, provided the standards of the U.S.P. and N.F. as established shall be fair and reasonable and that they can be met and attained as an average condition in the usual supply.

The present conditions with reference to the use and abuse of habit-forming drugs must carefully be considered and some means devised, by enactment of a National character, whereby the sale of all narcotic and habit-forming drugs in interstate commerce to others than those licensed to prescribe and dispense shall be completely stopped.

The bills proposing to establish a Department of Public Health should be amended so as to provide for a bureau of pharmacy.

With reference to the sale of alcoholic beverages, pharmacists should recognize that the time has arrived when it has become necessary for them to clearly establish their position in the eye of the public that they are pharmacists, and not rum sellers. They should be willing to eliminate from their business all sales of alcoholic beverages for any purpose whatsoever.

The bill to regulate the manufacture and sale of smoking opium is not rigid enough, it should provide for the abolishment of all such practices and provide heavy penalties in each and every case.

The bill providing for the regulation of the sale of habit-forming drugs in interstate commerce, whereby the sale of narcotic and habit-forming drugs interstate commerce can be better regulated and controlled, should be supported, it should be the aim of every pharmacist to put a stop to the sale of all such drugs except for legitimate purposes and under proper regulation.

The following is an abstract of the Report of the Committee on Weights and Measures:

Dr. S. W. Stratton, Director of the U. S. Bureau of Standards, Department of Commerce and Labor, Washington, D. C., furnished the chairman, at his request, a pamphlet on "The International Metric System of Weights and Measures," which was expressly prepared to answer some of the more simple questions addressed to the Bureau of Standards in regard to the metric system and its use. This pamphlet gives a concise history of the metric system, the names of the countries giving governmental support to the system, a synopsis of the system, and tables and diagrams showing a comparison of metric and customary units. And it is believed that this pamphlet would furnish an excellent basis for an article intended for educational purposes, whether circulated among pharmacists, physicians or others.

The Bureau of Standards has also gotten out a large chart showing the relation of the three metric units to one another, and in turn to the customary units employed. This chart would be especially useful in schools of pharmacy and medicine, and in other educational institutions where the subject of weights and measures is taught.

In fact, the chairman is of the opinion that most effective educational work leading to the general approval of the metric system can be accomplished by getting teachers in the public schools to lay more stress on the advantages of the metric system, and to give practical exercises using the actual measures and weights. In fact, the question of the adoption of the metric system universally in the United States could not long be delayed when once the pupils in our schools have learned to actually use metric weights and measures.

It is rather remarkable that, as shown in the pamphlet already referred to, when the use of the metric system is required in the Medical Departments of the Army and Navy, and in the U. S. Public Health and Marine-Hospital Service, and beside legalized in the Philippine Islands and made

obligatory in Porto Rico, there has been adopted in the Senate of the U. S. resolution entitled S. J. Res. 37 (Congressional Record, March 11, p. 3121), which is now under consideration by the Committee on Printing of the House of Representatives. This resolution provides that all documents, papers, etc., published by the Government of the United States be printed in the English language and would require that wherever references to metric weights and measures, centigrade thermometer and similar standards are used, the equivalent in the English standard be given.

This resolution scarcely needs other comment than to say that the necessity exists for guarding the progress that has already been made.

A similar back tendency in certain directions is shown by a recent editorial in *American Medicine* (January, 1910, p. 7) on "The Tyranny of the Metric Advocates and French Metric Tyranny." While the percentage of physicians who actually use the metric system in prescription writing is very small, it is probable that the majority of them recognize its advantages, and hence it may be taken for granted that this editorial will not have any real influence in hindering progress.

As showing what may be done by local branches of the A. Ph. A. attention is called to the action of the Chicago Branch which proposed two resolutions for submission to the National Convention of City Sealers which met in Washington on February 25 (See A. Ph. A. Bulletin, February, 1910).

A. B. STEVENS,  
CHARLES E. CASPARI,  
C. S. BRINTON,  
PHILIP ASHER,  
HENRY KRAEMER, Chairman.

One of the interesting and instructive features of the meeting was an exhibit of medicinal plants which was planned by President Rusby and largely contributed to by him. Dr. R. H. True, of the Bureau of Plant Industry of the U. S. Department of Agriculture, also sent a number of interesting plants from the Arlington drug farm of the government. Support was also received through the specimens contributed by Messrs. Eli Lilly & Co., Prof. E. V. Howell, University of North Carolina Department of Pharmacy, Professor Sayre of the University of Kansas and Professor Kraemer of the Philadelphia College of Pharmacy. With the exception of the specimens of hydrastis growing in soil and brought to the meeting by Professor Kraemer, all of the plants were placed in jars containing water and retained their fresh condition during the greater portion of the meeting. Quite a number of the specimens represented the leafy branches of the plant and gave rather a good idea of the nature of the plants. The following is an attempt



to give a nearly complete list of the plants which were exhibited and is published as it may be suggestive for use in connection with future exhibits.

Aconitum Napellus, Acorus Calamus, Achillea millefolium, Aesculus glabra, Aralia nudicaulis, Arctium Lappa, Aristolochia Serpentaria, Artemisia Absinthium, Arisaema triphyllum, Asarum reflexum, Asclepias tuberosa, Baptisia tinctoria, Brauneria (Echinacea) pallida, B. purpurea, Calendula officinalis, Capsella Bursa-pastoris, Carum Carvi, Chamaelirium carolinianum, Cercis canadensis, Chelone glabra, Cimicifuga racemosa, Cinnamomum zeylanicum, Conium maculatum, Convallaria majalis, Cornus florida, Cornus florida variety purpurea, Dryopteris marginalis, Equisetum hyemale, Eriodictyon californicum, Euonymus atropurpureus, Foeniculum vulgare, Gelsemium sempervirens, Geranium maculatum, Glechoma hederacea, Glycyrrhiza glabra, Gnaphalium obtusifolium, Hepatica acuta and H. triloba, Hydrangea arborescens, Hydrastis canadensis, Hyoscyamus niger, Inula Helenium, Iris versicolor, Jeffersonia diphylla, Leptamnium virginianum, Levisiticum officinale, Melissa officinalis, Mentha crispa, M. longifolia, M. piperita and M. spicata, Monarda fistulosa, Nepeta Cataria, Panax quinquefolium, Parthenocissus quinquefolia, Passiflora caerulea, Phytolacca decandra, Piper nigrum, Phlox carolina and P. ovata, Plantago major, Polygala Senega, Podophyllum peltatum, Prunus serotina, Pycnanthemum (Koellia) albescens, Quercus alba, Rhus glabra, Rubia tinctorum, Rumex crispus and R. obtusifolius, Salix alba, Salvia officinalis, Saponaria officinalis, Sassafras officinale, Scopolia carniolica, Senecio aureus, Spathyema foetida, Tanacetum vulgare, Thea sinensis, Trillium erectum, Taraxacum officinale, Triosteum perfoliatum and T. angustifolium, Valeriana officinalis, Vanilla planifolia, Veratrum viride, Verbascum thapsus, Viburnum prunifolium, Xanthorrhiza apiifolia.

A Committee on Editing was appointed to consider the framing of certain rules in regard to the use of titles and academic degrees in connection with the names of members to be printed in the Proceedings and also to agree on common editorial forms. These rules are to be applied on all the publications of the A. Ph. A., and it was further recommended that outside associations appoint delegates to confer with this Committee in order that there may be unison in the general manner of editing pharmaceutical publications in this country. President Rusby appointed the fol-

lowing members on this Committee: H. F. Taylor, C. S. N. Hallberg, C. A. Mayo, F. B. Hays and Henry Kraemer.

William B. Day, Chairman of the Committee on Membership, recommended the appointment of an official delegate of the A. Ph. A. to each of the meetings of the various State Pharmaceutical Associations who is to be requested to be present at the opening meeting of each of the State Associations. This recommendation was adopted and ought to be a means of directing attention to the work of the A. Ph. A. and of increasing its membership and should besides receive the support of all the members of the various State pharmaceutical associations.

The following reports were also received: the Committee on Reorganization, C. S. N. Hallberg, Chairman; the Committee on Branches, C. A. Mayo, Chairman; the Committee on the William Procter, Jr., Monument Fund, John F. Hancock, Chairman; the Committee on Publicity, F. B. Hays, Chairman; the Committee on the Status of Pharmacy in the Army and Navy, George F. Payne, Chairman.

The Committee on National Formulary through its Chairman, C. Lewis Diehl, presented a report which indicated the progress of the work and showed close co-operation with the members of the medical profession and the Committee on Unofficial Standards of A. Ph. A. The Association voted to allow a sum not exceeding \$1000.00 for the use of the Committee in making a line of preparations which shall become the property of the Association and be of use for purposes of reference.

After the presentation of the report of the Committee on National Formulary it was moved by George M. Beringer that an honorarium of \$50 be voted M. I. Wilbert for the extra services which he voluntarily rendered as a member of the Committee by having mimeographed copies made of the various circular letters and committee reports. This motion was at first approved by the Association, but later Mr. Beringer asked to reconsider the action taken, as Mr. Wilbert stated that on account of his being a government employe he could not accept the honorarium. After some additional discussion it was suggested that a vote of thanks to Surgeon-General Wyman, for his willingness to co-operate in the perfecting of the U.S.P. and the N.F., would be the more appropriate method of showing the appreciation of the work done

in connection with the Public Health and Marine Hospital Service. A resolution of this nature was then passed unanimously.

The final session of the Association continued till nearly 7 o'clock on Saturday afternoon. It was announced that Mr. Ewen McIntyre had been elected Honorary President. The session was concluded with the installation of the following officers-elect for 1910-1911: President, Eugene G. Eberle; First Vice-President, William B. Day; Second Vice-President, Otto F. Clause; Third Vice-President, Leonard A. Seltzer; Treasurer, H. M. Whelpley; Reporter on Progress of Pharmacy, C. Lewis Diehl; and General Secretary, Charles Caspari, Jr.

With this was concluded a meeting which will always stand out in the recollection of the members on account of its pleasant associations and the accomplishment of a vast amount of work.

#### SECTIONAL MEETINGS.

Simultaneous sessions of the several sections continued throughout the meeting. The program for the Section on Scientific Papers as published in the May *Bulletin of the A. Ph. A.* was strictly adhered to, thus making it possible for those in attendance to know what was being done in at least this one section.

The *Scientific Section*, with M. I. Wilbert as Chairman, held six sessions during which about 50 original communications were read and discussed. The Chairman's address was devoted to a consideration of lines of investigation and of fields of inquiry which might well claim our attention as it relates to the "uplift movement" in pharmacy. It included a discussion of the following subjects: (a) the pharmacist and the public health, (b) lost opportunities, (c) the coming revision of the U.S.P. and (d) the coming era in pharmacy. The whole of one session was devoted to the consideration of the report of the A. Ph. A. Committee on the U. S. Pharmacopœia. Thirty-two recommendations were discussed and finally approved by the Association and several of them were finally incorporated in the "General Principles to be followed in Revising the Pharmacopœia" adopted by the U. S. Pharmacopœial Convention.

The symposium on Physiological Testing was one of the important events of the meeting. The papers and discussion were suggestive, inspiring and forceful. One of the results of this symposium was the appointment of a Committee on Physiologic

Assays by the Association to consist of experts whose duty it will be to coördinate the various methods of biological assays and to propose standard methods. President Rusby subsequently appointed as members of this Committee: E. M. Houghton, Reid Hunt, H. C. Wood, Jr., R. A. Hatcher, Torald Sollmann and A. C. Crawford.

The Ebert Prize was awarded to H. M. Gordin for his papers of last year as well as his numerous scientific papers to the Association. The Committee on Drug Market, through the Chairman, E. L. Patch, presented a valuable report similar to those received by the Association for some years past. The officers-elect of the Scientific Section are Chairman, A. H. Clark; and Secretary, Wm. O. Richtmann.

*The Section on Practical Pharmacy and Dispensing* held three sessions. The Chairman, Mr. Otto Raubenheimer, in his address reminded the members of the rôle of eminent pharmacists, chemists, pharmacognosists and scientists who were born a hundred years ago and said that shortly there would be celebrated the centenary of the discovery of the most important alkaloids and that in about ten years the centenary of the oldest College of Pharmacy in the United States would also be celebrated. He also directed the attention of pharmacists to those studies and practices which would enable them to keep abreast of the times and to possess the necessary pharmaceutical knowledge which would assist them in doing their share for the protection of the patient.

One of the interesting sessions of this section was that devoted to a "symposium on the most important pharmacopœias of the world." While the greatest benefit must accrue to those who had an opportunity of seeing the pharmacopœias and examining them as well as participating in the discussions it would be indeed fortunate if the symposium of papers could be published as a separate pamphlet or at least together in one number of the *Bulletin of the A. Ph. A.* There were twenty-five papers presented, and one session was devoted entirely to a comparison of the most important groups of galenicals of the more important pharmacopœias with those of the U. S. Pharmacopœia and National Formulary, which was illustrated with specimens. The officers-elect of this section for the year 1910-11 are: Chairman, Carl Saalbach and Secretary, P. Henry Utech.

*The Section on Education and Legislation* held three sessions and as in the previous sections mentioned the interest was main-



tained up to the time for adjournment. The address of the Chairman, Charles H. LaWall was upon the subject of Education and Pharmacy and is published in full in the *American Druggist* for May 9, 1910, p. 288. Nearly twenty-five papers were presented in addition to which there was a joint session of the section with the National Association of Boards of Pharmacy and American Conference of Pharmaceutical Faculties.

The following officers of this section were elected for the ensuing year: Chairman, Charles W. Johnson; Secretary, W. J. Teeters; Associates, J. W. Sturmer, Philip Asher and J. C. Wallace.

*The Historical Section* held a single session with the Chairman, E. G. Eberle, in the chair. To the student of the Association and he who is the veteran in matters pharmaceutical these sessions are acknowledged to be to-day an essential part of the work of the Association. The papers of E. V. Howell on the pioneer botanists of the United States are always stimulating and refreshing. The letters of great pharmacists, the historical data relating to the Boards of Pharmacy and the State Pharmaceutical Associations, and the papers on historical subjects, which are pouring into the Association each year require that the Association very soon enter upon some plan for the erection of a permanent building where these documents may be conserved and made available to the members.

The Historian, Edward Kremers, presented a report in which he again recommended the creation of the office of Librarian and suggested "that the numerous officers of the Association file such portions of their correspondence and other documents, as might be of value, with the Historian, when they are through with this material." He also suggested that some steps be taken to secure the deposit and permanent care of the valuable documents that must have been accumulated by the chairmen of the several revision committees of the U. S. Pharmacopœia in some place where they will be generally available both to the medical and pharmaceutical professions. The officers-elect of the Historical Section for 1910-1911 are: Chairman, J. L. Lemberger; and Secretary, Otto Raubheimer.

The *Commercial Section* held two sessions with the Chairman Waldo M. Bowman presiding. The chairman's address dealt with the subject of the "Purification of Commercial Pharmacy," in which he directed attention to "the need of elevating the standards

of commercial practice in pharmacy and of purifying it of the evils that encompass it." Twelve papers were presented to the section and that some of these seemed to belong to one or the other of the other sections, furnishes an illustration of the difficulty in drawing the lines between the work of the several sections.

The following are the officers of the Commercial Section for the ensuing year: Chairman, F. M. Apple; Secretary, B. E. Pritchard; Associates, Sydney Yeomans and C. M. Ford.

The *Program of Entertainment* under the charge of the Local Secretary, T. A. Miller, included a luncheon at Lakeside Park; a reception, tendered the Association by His Excellency, Wm. H. Mann, at the Governor's mansion; a card party for the ladies at the Woman's Club, and many courtesies including special trips to historic points in and around the city of Richmond.

H. K.

#### PHILADELPHIA COLLEGE OF PHARMACY.

The eighty-ninth annual commencement of the Philadelphia College of Pharmacy was held in the American Academy of Music on Thursday evening, May 26. After prayer by Rev. Llewellyn N. Caley, the degrees were conferred by President Howard B. French.

The following are the names of those who received the degree of Doctor in Pharmacy (P.D.), together with the subjects:

<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Amsterdam, Peter,	Cassia Bark and Cinnamons (official)	Russia
Bartholomew, Samuel	The Volumetric Determination of	
Howard,	Sodium Borate,	Pennsylvania
Baun, William David,	Cinchona and its Bast Fibres,	Pennsylvania
Beck, Jay Dana,	A Simple Apparatus for the Recovery of Alcohol in the Retail Pharmacy,	Pennsylvania
Blumberg, Joseph,	Zinc Oxide,	Pennsylvania
Bolton, Stephen Dwight,	The Manufacture of Extract of Vanilla and its Importance in Pharmacy,	New York
Borneman, Warren		
Roland,	Potassii Bitartras,	Pennsylvania
Bose, Charles Henry,	Sambucus Canadensis,	Pennsylvania
Breen, James Stanley,	A Process for Determining the Value of Soap,	Pennsylvania

<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Bringman, Merle Stoles,	Blood and Tests for Blood,	Pennsylvania
Brooks, Jay William,	The A.O.A.C. Standards as applied to Belladonna,	New York
Butt, Luke Thomas,	Pepsin,	Pennsylvania
Chapman, George Fulmer,	Aqua Hydrogenii Dioxidi,	Pennsylvania
Connelly, Lester Cleveland,	The Advantages of the Compound Microscope in the Examination of Powdered Drugs,	Pennsylvania
Deck, Roy,	H <sub>2</sub> O <sub>2</sub> as sold by Druggists,	Pennsylvania
DeHaven, Henry Vernon,	Sandalwood,	Pennsylvania
Dilatush, Howard Bur-	Phenol,	New Jersey
Driver, Walter,	A Quick Method for Filling Bottles,	Utah
Durbin, William Stacey,	Rhamnus Purshiana,	
Eberly, Norman Elias,	Hydrastis,	Pennsylvania
Eby, Maurice Herr,	Prescription Difficulties,	Pennsylvania
Emlet, John Matthias,	Ferri Sulphas Exsiccatus,	Pennsylvania
Feinstein (Miss) Anna (P.C.),	Microscopical Examination of Pow- dered Rhubarb,	Russia
Gibney, Edward Paul,	Soluble Bismuth and Sodium Tar- trate,	Pennsylvania
Goodwin, James Jeffries,	Assay of Ferrum Reductum,	Kentucky
Greenberg, Hyman,	Improved Method for Prepared Cas- tor Oil,	Pennsylvania
Greene, William Robert,	Antiseptic Properties of Iron,	Pennsylvania
Greiner, Chloe Earl,	Liquor Potassii Hydroxidi,	Ohio
Griesener, Fred,	Liquor Sodæ Chlorinata,	Pennsylvania
Grom, Roland Bismarck,	Evolution and Pharmacy,	New Jersey
Grove, Norbert Harri- son,	Chromium Trioxide,	Pennsylvania
Guenther, Harold Dick- inson,	Percentage Loss or Gain in Weight of U.S.P. Chemicals at Store Tem- perature,	Pennsylvania
Harris, William Clyde,	Arsenious Iodide,	Pennsylvania
Harting, Alfred Martin,	Solution Iron Peptonate with Man- ganese,	Maryland
Henkel, Joseph Victor,	Monohydrated Sodium Carbonate,	Pennsylvania
Henrie, Arthur Cecil,	Analytical Methods for the Pharma- cist,	Pennsylvania
Hickory, Edward Cal- vin,	Toilet Creams of the Casein and So- dium Stearate Types,	Pennsylvania
Honsaker, Charles Coy,	Phenolphthalein,	Pennsylvania
Horn, Charles Lewis,	Liquor Ferri Iodidi N.F. 3d,	Pennsylvania

<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Hulick, George Bercaw,	Spiritus Ætheris Nitrosi,	Pennsylvania
Jones, Ellsworth R.,	Rhamnus Purshiana,	Pennsylvania
Kehr, Erney Cornelius,	Glycerite of the Phosphates of Iron, Quinine and Strychnine,	Pennsylvania
Keister, Vastine Atkin- son,	Bacterium Lactici Acidi,	Virginia
Keys, William Wallace,	Commercial Varieties of Rhubarb,	Pennsylvania
Kniley, Eugene Walker,	Sodii Sulphus,	Pennsylvania
Kooker, John Leedom,	Caffea,	Pennsylvania
Korb, Edward Michael,	Zinc Oxide,	Pennsylvania
Kramer, James,	Syrup of Ferrous Iodide,	Pennsylvania
Lamb, Sylvan Deering,	Magma Bismuthi,	Indiana
Lang, Charles Nicholas,	The Collection, Preparation and Preservation of a local Herbarium,	Pennsylvania
Laros, William Jonas,	Window Dressing and its Value,	Pennsylvania
Levan, George B.,	The Preservation of Vegetable Drugs,	Pennsylvania
Lounds, Albert Edward,	Permanency of Glycerophosphates,	Florida
Lounsbury, William At- kinson,	The Preservation of Syrup of Fer- rous Iodide,	New Jersey
Loveless, Earl Martin,	The Assay and Micro-Chemistry of Strophanthus,	Pennsylvania
McAninch, Harry El- mer,	Liquor Magnesii Citratis,	Pennsylvania
McCarty, Raymond		
Welles,	Pepsin,	Pennsylvania
McCutcheon, Thomas Edward,	Aloes, Identification, Adulteration and Tests,	Pennsylvania
McGonigal, John Aloy- sius,	History of Opium,	Pennsylvania
McMillen, Donald At- lee,	The Effect of Heat on the Alkaloidal Assay of Opium,	Pennsylvania
Mallas, Maurice Louis,	Collection of the Medicinal Barks of Commerce,	Pennsylvania
Marshall, Thomas Car- penter,	Elixir Digestivum Comp,	Pennsylvania
Metcalf, Elliott Harri- son,	Pancreatin,	Connecticut
Metzler, Robert,	Hepatica,	Pennsylvania
Mohn, Emory Shinkle.	Potassium Iodide and Potassium Bromide,	Pennsylvania
Morgan (Miss) Lula A. (P.C.),	Acidum Boricum,	Pennsylvania
Moser, Earl Spencer,	Sapo Mollis,	Pennsylvania
Mueller, Sister Bertha,	Digitalis,	Michigan



<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Mutty, Joseph Edwin,	Liquid Extract of China "Dutch,"	Maine
Naly (Miss) Sarah L. (Ph.G.),	Microscopical Laboratory,	Pennsylvania
Owens, Evan Richard,	Viburnum Prunifolium,	Pennsylvania
Pettyjohn, Harry Jack- son,	Colocynthis,	Delaware
Press, Henry William,	The Proper Time to Collect Roots and Rhizomes,	Pennsylvania
Raines, Edward William,	Bacteriological Examination of Gela- tin,	Illinois
Ritchey, George Edgar,	Kaolinum,	Pennsylvania
Ritchey, Jacob C. Leh- man,	Hydrastis Canadensis,	Pennsylvania
Rodes, Zebulon Harri- son,	Ammonium Sulpho-Ichthyolate,	Pennsylvania
Roof, William George,	The Manufacture of Paper,	Pennsylvania
Rothenberger, Charles B.,	The Cultivation of Hydrastis Cana- densis,	Pennsylvania
Ruch, Walter Edward,	The Utility of Pharmacognosy,	New Jersey
Russell, Percy Reginald,	Milk of Magnesia,	Pennsylvania
Scargle, William,	A Practical System of Discounts for Pharmacists,	Pennsylvania
Schabacker, Horace Martin,	Pepsinum,	Pennsylvania
Schuehle, Christopher, Jr.,	Seed Dispersal,	Pennsylvania
Shelly, William Harri- son C.,	Phenolphthalein as a Cathartic,	Pennsylvania
Solomon, Roscoe,	Phenol,	Pennsylvania
Stratton, Ernest Ken- neth,	Casein	New Jersey
Topper, Louis LeRoy,	Saccharum,	Pennsylvania
Treichler, Frank Albert,	Sodium Benzoate,	Pennsylvania
Turner, Walter William,	Cannabis Indica,	Pennsylvania
Viner, Lewis,	Glycerinum,	Russia
Walton, John Carroll,	Essentia Pepsini,	Pennsylvania
Webb, Paul Carleton Hill,	Notes on the Histology and Chemis- try of Tonquin Wood,	Pennsylvania
Webb, Walter Nardin,	Olive Oil,	S. Carolina
Werner, Karl,	Vanilla Flavoring Extracts,	Pennsylvania
Wiesner, Joseph Frank- lin,	Potassii Bicarbonas,	Wisconsin
Willingmyre, Philip Shuster,	The Effect of Heat on Opium,	Pennsylvania

<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Wilson, John Herbert,	Some Special Tests for Valuation of Anthemis,	Pennsylvania
Wilson, Lewis Elmer,	Fluid Glycerite of Krameria,	Maine
Wilson, Robert James,	Precipitated Manganese Dioxide,	Pennsylvania
Wolfe, Claude Senft,	Elixir Aromaticum,	Pennsylvania
Workman, Edward Benjamin,	Magnesium Oxide,	Pennsylvania
Zelmanoff, David Solomon,	Sulphur Iodide,	Russia
Ziegler, Frank Loomis,	Calcium Orthosilicate,	Pennsylvania
Ziegler, John Edwin,	Oleum Cinnamomi,	Pennsylvania

The following are the names of those who received the degree of Pharmaceutical Chemist (P. C.), together with the subjects of their theses:

<i>Name.</i>	<i>Thesis.</i>	<i>State or Country.</i>
Bost, William Dale,	Liquor Plumbi Subacetatis,	N. Carolina
Cadwallader, Wayne,	Ferri Carbonas Saccharatus,	Pennsylvania
Calvin, William Ray,	Liquor Potassii Arsenitis,	Pennsylvania
Cooper, William Benjamin,	The Value of Efficiency of Greaseless Creams,	Pennsylvania
Costello (Miss), Mary O'Dea,	The Anatomy of Cactus,	Pennsylvania
Ferry (Miss), Fanny,	The Size of Globules in Various Emulsions,	Pennsylvania
Fleisher, Lewis,	Cork,	Pennsylvania
Henry, Carl Racine,	Liquor Sodii Phosphatis Compositus,	New York
Klopp, Wallace Ellwood,	The Commercial Varieties of Vanilla,	Pennsylvania
Lengel, James Petri,	Rhubarb,	Pennsylvania
Powell (Miss), Mary G.,	The Morphology of the Glandular Hairs of Humulus,	Pennsylvania
Sankey, Foster John,	Ammonia,	Pennsylvania
Schmidt (Miss), Selma L.,	The Testing of Balsam of Peru,	Ohio
Severa, Lumir,	Liquor Chlori Compositus,	Iowa
Siegel, Philip,	Precipitates in Alkaloidal Tinctures,	Colorado

The following were awarded certificates in the Pure Food and Drug Course: Harmon M. Sechler, Pennsylvania; and Ralph Thomas Ulrich, P.D., Pennsylvania.

There were 122 candidates for the degree *in course*, coming from the various States and countries as follows: Colorado, 1;

Connecticut, 1; Delaware, 1; Florida, 1; Illinois, 1; Indiana, 1; Iowa, 1; Kentucky, 1; Maine, 2; Maryland, 1; Michigan, 1; New Jersey, 5; New York, 3; North Carolina, 1; Ohio, 2; Pennsylvania, 91; Russia, 4; South Carolina, 1; Utah, 1; Virginia, 1; and Wisconsin, 1.

A brief but trenchant address to the graduating class was delivered by His Excellency, Hon. Edwin S. Stuart, Governor of Pennsylvania, in which he considered "Some of the Qualities that make for Success," dwelling particularly upon the importance of industry, perseverance, and integrity.

#### AWARD OF PRIZES.

The following students received the grade of distinguished: Sister Bertha Mueller and Walter E. Ruch. The grade of meritorious was attained by John A. McGonigal, Mary G. Powell, Zebulon H. Rodes and John E. Ziegler.

THE PROCTOR PRIZE, a gold medal and certificate, for the highest general average of the class with a meritorious thesis, was awarded to Sister Bertha Mueller, the presentation being made by President French.

THE WILLIAM B. WEBB MEMORIAL PRIZE, a gold medal and certificate offered for the highest general average in the branches of committee, operative pharmacy and specimens, was awarded to Sister Bertha Mueller, the presentation being made by W. L. Cliffe. The following graduates received honorable mention in connection therewith: John A. McGonigal and Zebulon H. Rodes.

THE MATERIA MEDICA PRIZE, \$25, offered by Prof. Clement B. Lowe, for the best examination in materia medica and in the recognition of materia medica specimens with a meritorious thesis, was awarded to Sister Bertha Mueller. The following graduates received honorable mention in connection therewith: Jay D. Beck, William R. Calvin, Lester C. Connelly, Charles L. Horn, Thomas E. McCutcheon, John A. McGonigal, Elliott H. Metcalf, Henry W. Press, Zebulon H. Rodes, Walter E. Ruch, Robert J. Wilson and John E. Ziegler.

THE MICROSCOPICAL RESEARCH PRIZE, a Zentmayer microscope, offered by Prof. Henry Kraemer, for the most meritorious thesis involving original microscopic work, was awarded to Sister Bertha Mueller. The following graduates received honorable mention in

connection therewith: Peter Amsterdam, William D. Baun, Jay W. Brooks, Norman E. Eberly, Vastine A. Keister, Wallace E. Klopp, Earl M. Loveless, Mary G. Powell, Edward W. Raines and Paul C. H. Webb.

THE ANALYTICAL CHEMISTRY PRIZE, \$25, offered by Prof. Frank X. Moerk, for the best work in qualitative and quantitative analysis, was awarded to Norman Elias Eberly. The following graduates received honorable mention in connection therewith: James J. Goodwin, Sister Bertha Mueller, Zebulon H. Rodes and Walter E. Ruch.

THE OPERATIVE PHARMACY PRIZE, \$20 in gold, offered by Prof. Joseph P. Remington, for the best examination in operative pharmacy, was awarded to Thomas Edward McCutcheon. The following graduates received honorable mention in connection therewith: Roy Deck, Arthur C. Henrie, John A. McGonigal, Sister Bertha Mueller, Joseph E. Mutty, Foster J. Sankey and Christopher Schuehle, Jr.

THE MAISCH PHARMACOGNOSY PRIZE, \$20 in gold, established by the late Jacob H. Redsecker, of Lebanon, Pa., and continued as a memorial by his nephew, Jacob Redsecker Beetem, for his-  
tological knowledge of drugs, was awarded to Sister Bertha Mueller, the presentation being made by J. L. Lemberger. The following graduates received honorable mention in connection therewith: William R. Calvin, Charles L. Horn, Thomas E. McCutcheon, John A. McGonigal, Walter E. Ruch and John E. Ziegler.

THE MAISCH BOTANY PRIZE, \$20, offered by Mr. Joseph Jacobs, of Atlanta, Ga., for the best herbarium collection of plants, was awarded to Charles Nicholas Lang, the presentation being made by E. L. Newcomb. The following graduate received honorable mention in connection therewith: George B. Levan.

THE THEORETICAL PHARMACY PRIZE, a Troemner Agate Prescription Balance, established by the late Mahlon N. Kline, for the best examination in theory and practice of pharmacy, was awarded to John Aloysius McGonigal, the presentation being made by his son, C. Mahlon Kline. The following graduates received honorable mention in connection therewith: Peter Amsterdam, Sister Bertha Mueller and Mary G. Powell.

THE COMMERCIAL TRAINING PRIZE, \$20 in gold, offered by Prof. Joseph P. Remington to the graduate who passed the best examination in commercial training at the final examination for



the degree, was awarded to Walter Ruch, the presentation being made by E. Fullerton Cók. The following graduates received honorable mention in connection therewith: Jay D. Beck, Jay W. Brooks, Wayne Cadawallader, William R. Calvin, Roy Deck, Walter Driver, John M. Emlet, Fred Griesemer, Norbet H. Grove, Alfred M. Harting, Edwin C. Hickory, Charles L. Horn, Wallace E. Klopp, Thomas E. McCutcheon, Sister Bertha Mueller, Joseph E. Mutty, Harry J. Pettyjohn, Mary G. Powell, Lumir Severa, Frank L. Ziegler and John E. Ziegler.

THE INSTRUCTORS' PRIZE, \$20, offered by the Instructors of the College for the highest term average in the branches of pharmacy, chemistry and materia medica, was awarded to Walter E. Ruch, the presentation being made by F. P. Stroup. The following graduates received honorable mention in connection therewith: Jay W. Brooks, William R. Calvin, John M. Emlet, James J. Goodwin, Charles L. Horn, George B. Levan, John A. McGonigal, Maurice L. Mallas, Sister Bertha Mueller, Henry W. Press, Zebulon H. Rodes, Christopher Schuehle, Jr., Frank L. Ziegler and John E. Ziegler.

THE PHARMACY QUIZ PRIZE, one year's membership in the American Pharmaceutical Association, offered by Prof. Charles H. LaWall for the best term work in theory and practice of pharmacy, was awarded to Walter Ruch. The following graduates received honorable mention in connection therewith: George B. Levan and Zebulon H. Rodes.

THE KAPPA PSI FRATERNITY PRIZE, a gold medal, offered by the Eta Chapter of the Kappa Psi Fraternity to the graduate making the highest general average during his or her senior year at the College, was awarded to Sister Bertha Mueller, the presentation being made by Professor Remington. The following graduates received honorable mention in connection therewith: John A. McGonigal, Mary G. Powell, Zebulon H. Rodes, Walter E. Ruch and John E. Ziegler.

THE ATHLETIC PRIZE, a silver loving cup, offered by Henry S. Godshall, P.D., and John J. Bridgeman, P.D., to the member of the graduating class who, at commencement, stands with the greatest number of points in athletics to his credit and has obtained the highest general average amongst those participating in athletics at the College, was awarded to Evan Richard Owens, the presentation being made by Dr. R. Tait McKenzie,

Director of Physical Education in the University of Pennsylvania. The following graduate received honorable mention in connection therewith: John M. Emlet.

#### COMPLIMENTARY SUPPER.

A complimentary supper to the graduating class was given by the Faculty on Wednesday evening, May 25. In addition to the toast by the members of the Faculty and Instructors, brief responses were made by some 30 members of the graduating class representing different sections of the United States and foreign countries.

#### BACCALAUREATE SERMON.

The bacculaureate sermon was preached by the Rev. David M. Steele in the Church of St. Luke and the Epiphany on Sunday, May 22, at four o'clock.

#### BANQUET.

A banquet was tendered the alumni of the Philadelphia College of Pharmacy who were recently selected members of the General Committee of Revision of the U. S. Pharmacopœia at the Union League following the graduation exercises on Thursday evening, May 26. President Howard B. French presided, and among the invited guests was Governor Edwin S. Stuart.

#### ALUMNI ASSOCIATION.

The Alumni Association held its forty-sixth annual meeting on Monday, May 23. The annual banquet was held on Tuesday evening, May 24, at the Hotel Walton and was attended by nearly 250 members and invited guests. The details of the events of the Alumni Association will be published in the *Alumni Report*.

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### PROCEEDINGS OF THE ELEVENTH ANNUAL MEETING OF THE AMERICAN CONFERENCE OF PHAR- MACEUTICAL FACULTIES HELD AT RICHMOND, VIRGINIA.

Twenty-six colleges of pharmacy were represented by delegates at this the eleventh annual meeting held May 2-7, 1910. On account of the death of the president of the Conference, Wm.

M. Searby, the vice-president, E. H. La Pierre, presided at the meetings.

The vice-president in his address called particular attention to the growth of the Conference from seventeen schools at its organization in 1900 at Richmond, Va., to thirty-three schools now holding membership.

The report of the chairman of the executive committee showed that the Conference was doing much toward assisting in raising the standards of pharmaceutical education.

The pharmaceutical syllabus was carefully considered and the Conference voted to approve its general scope and purposes. The following were elected to represent the Conference on the general syllabus committee: J. H. Beal, H. H. Rusby, J. O. Schlotterbeck, J. A. Koch, W. C. Anderson, C. B. Lowe, and H. V. Army.

The by-laws of the constitution were amended so as to provide that one year of high-school shall be the minimum requirement for entrance to all schools holding membership in the Conference.

Prof. J. T. McGill, of Vanderbilt University, read a paper on "The High School in the Southern States." The aim of Professor McGill's paper was to show that the southern states had ample high-school facilities to prepare students to meet the minimum requirement of one year's high-school work.

The following persons were elected as officers of the Conference for the year 1910-1911: President, J. O. Schlotterbeck, University of Michigan, Ann Arbor; Vice-President, W. J. Teeters, State University of Iowa, Iowa City; Secretary-Treasurer, Charles W. Johnson, University of Washington, Seattle; Executive Committee: Chairman, J. A. Koch, Pittsburg College of Pharmacy, Pittsburg; F. P. Stroup, Philadelphia College of Pharmacy, Philadelphia; E. G. Eberle, Baylor University, College of Pharmacy, Dallas, Texas; E. H. La Pierre, Massachusetts College of Pharmacy, Boston; J. M. Good, St. Louis College of Pharmacy, St. Louis.

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#### NEW ESSENTIAL OILS.\*

*Oil of Cinnamomum Tamala.*—Besides other low-grade *Cinnamomum*-species, it is especially *Cinnamomum Tamala* (Nees et Eberm.), a tree of medium size, growing plentifully in Southern Asia, which yields "Mutterzimt," *Cassia Lignea*, or Woodcassia,

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\*From Semi-Annual Report of Schimmel & Co., April, 1910, pp. 122-124.

termed by the retail trade simply *Cassia*. The leaves of the tree are still used medicinally in the East Indies; in former years they were also met with in commerce (the narrow *Folia Malabathri*) but they are now obsolete. The leaves contain an essential oil of which we recently received a sample, which had been distilled by Mr. I. H. Burkill, of Calcutta. The oil was of a lemon-yellow colour, and had a clovelike, at the same time slightly peppery, odour. It possessed the following constants:  $d_{15}^{\circ} 1.0257$ ,  $^{\circ}D + 16^{\circ} 37'$ ,  $^{\circ}D_{20}^{\circ} 1.52596$ ; phenol-content 78 per cent., soluble in 1,2 volumes and over of 70 per cent. alcohol. The phenols consisted of eugenol (m. p. of the benzoyl compound  $69^{\circ}$ ). When freed from phenols, the oil had the high optical rotation  $^{\circ}D + 66^{\circ} 40'$  and yielded a solid nitrite which, when recrystallised from ethyl acetate melted at  $113$  to  $114^{\circ}$ . It contained therefore d- $\alpha$ -phellandrene. In respect of its high eugenol content it is closely allied to the ordinary oil from Ceylon cinnamon leaves.

*Oil of Mentha silvestris*.—An oil of *Mentha silvestris* L., prepared in Cyprus, was found to possess the following properties:  $d_{15}^{\circ} 0.9701$ ,  $^{\circ}D + 31^{\circ} 30'$ ,  $^{\circ}D_{20}^{\circ} 1.49544$ , acid no. 2,4, ester no. 20,9, ester no. after acetyl. 171,4, soluble in 3 vols. of 70 per cent. alcohol; (the diluted solution showed slight opalescence;) faintly mint-like odour; yellow colour. It is obvious that the saponification number of 171,4 after acetylation of the oil cannot in this case be indicative of the menthol content, which, judging by this factor, should have been 54,8 per cent.; for as a matter of fact the sample contained but little menthol. The mint-like odour was chiefly due to the presence of pulegone, of which the oil contained 40 per cent. (isolated with neutral sulphite of sodium). In addition to this a phenol (probably carvacrol) could be detected, from which it is to be supposed that this, also, would become esterified and would help to swell the acetylation value. Owing to the simultaneous occurrence in it of menthol, pulegone and a phenol, the oil cannot be used either as peppermint oil or as European pennyroyal or origanum oil. It is differentiated from oil of peppermint by its much higher specific gravity and by its pronounced dextrorotatory power. We received the sample from the Imperial Institute in London.



# THE AMERICAN JOURNAL OF PHARMACY

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*JULY, 1910*

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## INTERNATIONAL STANDARDS—THE DESIRABILITY OF DEVELOPING INTERNATIONAL UNIFORMITY IN NOMENCLATURE AND STRENGTH OF WIDELY USED MEDICINES.\*

BY M. I. WILBERT.

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For many decades the better informed men in pharmacy as well as medicine have endeavored to create more widespread interest in the need for generally acceptable uniform names and standards of strength for medicinal preparations.

This need for universal standards, first recognized in the early years of the nineteenth century, was more fully appreciated when steam and electricity began to annihilate space and time so that the previously formidable obstacle of distance no longer sufficed to keep the people of different countries from intermingling.

It was pointed out at a very early period that the lack of uniformity in nomenclature and standards of strength for pharmaceutical preparations constitutes a real source of danger to the traveller, but it was soon recognized that the direct danger to the individual is of much less import than the indirect effect on the progress of the sciences of medicine.

This indirect effect has evidenced itself in many ways, not the least important of which has been the hindrance that the evident variation in name and strength of pharmaceutical preparations has been to the development of a rational materia medica and the in-

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\* Prepared for the Congress on Hygiene and Medicine, held in the City of Buenos Ayres, Argentine, May, 1910.

fluence it has had on the increase of proprietary medicaments with their attending misrepresentation and fraud.

The growth of intercommunication and commerce which followed the Napoleonic wars early in the nineteenth century led to repeated attempts to secure greater uniformity in strength and nomenclature of medicaments. One of these earlier attempts is reflected by a conspectus of the several then existing pharmacopœias, dispensaries and formularies of the world, compiled by A. J. L. Jourdan, and published in 1828. A second edition of this work, in two volumes, comprising a total of more than 1450 pages, was published in 1840.

The first edition included a review of 35 official pharmacopœias and 18 formularies while the second edition included 42 pharmacopœias and 31 formularies.

Largely due to the initiative of Professor George Dragendorff, then just at the beginning of his eventful career, an International Pharmaceutical Congress was held at Brunswick, Germany, in 1865, to discuss the possibility of evolving greater uniformity in pharmacopœial requirements. This initial congress was attended by delegates from Germany, Russia, Austria, France, and Sweden. In discussing the practicability of evolving an international pharmacopœia it was pointed out that uniformity in nomenclature and in the formulæ of pharmacopœial galenicals could readily be attained if at the periodical revision of the various pharmacopœias such changes were seriously attempted.

At the second congress, held in Paris in 1867, it was proposed to compile and publish a code that would serve as a basis for international standards, and at the third congress, held in Vienna in September, 1869, it was announced that the Pharmaceutical Society of Paris had volunteered to compile a comparative epitome of national pharmacopœias showing the differences existing at that time in regard to the nomenclature, composition and strength of galenical preparations. This compilation was to be submitted to the next international congress, and, it was expected, would form the basis for an agreement to serve as a guide in future revisions of the several national pharmacopœias.

Largely because of the Franco-German war the fourth international congress was not held at the time specified and it was not until 3 years later, in 1874, that the congress met in St. Petersburg.

The Society of Pharmacy of Paris presented the promised epit-

ome of the several national pharmacopœias and also an outline of suggestions for further discussion. It was specifically pointed out that: "The international pharmacopœia is not to supersede national pharmacopœias but it is desirable that in the construction of the latter the fundamental principles of the international pharmacopœia should be adopted."

It was further agreed that the language of the proposed code should be Latin, that the metric system should be adopted in the formulæ of the preparations, that the nomenclature be uniform, that galenical preparations, such as tinctures, extracts, etc., should be made as nearly uniform as possible, and that the maximum admissible amount of impurity in chemical preparations be stated.

This admittedly excellent ideal was never developed and at the fifth International Pharmaceutical Congress, held in London, 1881, it was learned that the manuscript that had been prepared by the Pharmaceutical Society of Paris was inadvertently destroyed by fire and that nothing of practical value had been accomplished in the interval.

Considerable impetus to the development of an international pharmacopœia was given by the "Universal Pharmacopœe" by Bruno Hirsh. The first edition of this compilation, published in 1887, included an epitome of all of the known national pharmacopœias. The second edition of the work, published in 1902, includes 4450 separate articles and an index covering 46 three-column pages.

Even a casual comparison of the compilation by Jourdan and the later one by Hirsh evidences the fact that the rapid dissemination of news and knowledge, the introduction of the metric system of weights and measures, the tendency to eliminate inert or useless materials from pharmacopœias, and the more frequent intercommunication between the people of widely separated countries have served to bring about a gradual approximation in the names and the strength of various medicaments.

On the other hand many of the agencies which have been instrumental in bringing about this approximation also tend to emphasize the still existing differences in the name and strength of widely used preparations.

The overconservatism manifested by the stay-at-home element in medicine and pharmacy is largely responsible for the lack of progress or of practical results from the several International Congresses held previous to 1900.

As has been pointed out repeatedly these congresses were international only in name, they were never well attended and the discussions and resolutions were futile because of their being altogether too comprehensive.

At the ninth International Pharmacopœial Congress, held in Paris in 1900, Professor A. Tschirch, of Berne, reviewed the efforts that had been made to develop an agreement to secure greater uniformity in the strength and nomenclature of widely used medicines and pointed out that the several congresses had proven to be impotent because they lacked the official standing that was necessary to make their conclusions effective.

He proposed that the ninth International Congress request the Belgian Government to arrange with other governments for a conference in Brussels, and to ask that all of the delegates appointed to attend such a conference have their proposals ready to lay before the meeting whenever this may be called. It was also suggested that the conference be restricted to the discussion of the name and strength of widely used potent medicaments.

The delegates appointed by their respective governments to attend this International Conference for the Unification of Pharmacopœial Formulæ for Potent Medicaments met in Brussels, September 15, 1902. The conference included delegates from the United States and from 18 European countries.

After fully discussing a variety of propositions the conclusions were finally embodied in the form of a protocol designating the nomenclature, strength and method of preparing the several medicaments.

This protocol was subscribed to by the delegates present and these signatures were subsequently ratified by the Diplomatic Representatives of the several governments, thus giving to this agreement the status of an international treaty.

For men who are really interested in the progress of medicine, the unanimity with which the provisions of the Brussels protocol have been embodied in the several national pharmacopœias has been a revelation as well as an inspiration.

For nearly a century it had been asserted that international uniformity in pharmaceutical preparations was impractical and that the several nations could never be induced to accept for inclusion in their pharmacopœias the dictates of outside influences. The futility of these assertions is amply demonstrated by the fact that within a



single decade the total compliances with the requirements of the Brussels protocol on the part of the leading pharmacopœias of the world have been increased from less than 50 per cent. in 1902 to 95 per cent. in 1910.

While European pharmacopœias, generally, have been brought well into compliance with the provisions of the Brussels protocol the national pharmacopœias now official in North and South America mostly antedate the Brussels Conference and are therefore not in accord with the requirements.

The variations in the strength of potent medicaments now existing in the pharmacopœias used in the several countries of North and South America are well illustrated by the appended table giving the requirements of the International Protocol and the comparative strength of the corresponding preparations in the several well known pharmacopœias that are either officially recognized or widely consulted in American countries.

Of the several pharmacopœias used on this Continent the French Codex, the Spanish Pharmacopœia, and the Pharmacopœia of Mexico comply fully with the protocol of the Brussels Conference, the Pharmacopœia of the United States complies fairly well with the several requirements, while the Pharmacopœias of Great Britain, of Argentina, of Venezuela, and of Chili antedate the Brussels Conference and differ rather widely in many respects from the provisions of the protocol adopted at that time.

One rather important variation manifested by the Pharmacopœias used in North America is due to the fact that English speaking pharmacists have been trained to measure rather than weigh pharmaceutical preparations. As is well known the latter is the accustomed practice on the Continent of Europe and throughout South America, and it may be necessary for American and English pharmacists to change their mode of making preparations before the proposed international standards can be fully complied with.

The desirability of developing a uniform nomenclature on this hemisphere is well illustrated by table 2 showing the titles used in the several pharmacopœias for 3 of the articles included in the Brussels protocol: Cocaine hydrochloride, Fowler's solution and fluidextract of ergot.

One difficulty in the way of developing Pan-American uniformity in the nomenclature of pharmacopœial substances is the fact that in Spanish-America Latin titles are considered as being of but second-

TABLE SHOWING COMPARATIVE STRENGTH OF PREPARATIONS OF POTENT MEDICAMENTS INCLUDED IN THE BRUSSELS CONFERENCE PROTOCOL AND IN THE SEVERAL PHARMACOPŒIAS USED IN NORTH AND SOUTH AMERICA.

	P. I. 1902	Ph. Brit. IV 1898 and B. P. C.	U. S. P. VIII 1905 and Spanish Edi- tion 1909	Ph. Mex. IV 1904	Ph. Fr. V 1908	Ph. Hisp. VII 1905	Ph. Venz. I 1898	Ph. Germ. IV 1900	Ph. Chili I 1886	Ph. Arg. I 1898
<i>Aconitum napellus</i> (L):										
Tinctura aconiti.	10	5w/v	10w/v	10	10	10	20	10	10	0
Menstruum	A70	A70	A7 + W3	A70	A70	A70	A60	A70	A60	.....
<i>Atropa belladonna</i> (L):										
Tinctura belladonnæ	10	0	10w/v	10	10	10	20	0	10	.....
Menstruum	A70	.....	Dil. A	A70	A70	A70	A60	.....	A60	.....
Extractum belladonnæ	A70	A70	A2 W1	A60	A70	A70	A60	W-A	A40	W
<i>Colchicum autumnale</i> (L):										
Tinctura colchici	10	20w/v	10w/v	10	10	10	20	10	10	20
Menstruum	A70	A45	A6 W4	A70	A70	A70	A60	A70	A60	A60
<i>Digitalis purpurea</i> (L):										
Tinctura digitalis	10	12 + 5w/v	10w/v	10	10	10	20	10	10	20
Menstruum	A70	A60	Dil. A	A70	A70	A70	A60	A70	A60	A60
<i>Uragoga ipecacuanhæ</i> (Baill):										
Tinctura ipecacuanhæ	10	0	0	10	10	10	20	0	20	.....
Menstruum	A70	.....	.....	A70	A70	A70	A60	.....	A60	A60
<i>Syrupus ipecacuanhæ</i>	1	2w/v	7	1	lex	1	1	1	2	1
<i>Hyoscyamus niger</i> (L):										
Tinctura hyoscyami	10	10w/v	10w/v	10	10	10	20	0	10	0
Menstruum	A70	A45	Dil. A	A70	A70	A70	A60	.....	A60	.....

[illegible]

TABLE SHOWING COMPARATIVE STRENGTH OF PREPARATIONS OF POTENT MEDICAMENTS INCLUDED IN THE BRUSSELS CONFERENCE PROTOCOL AND IN THE SEVERAL PHARMACOPŒIAS USED IN NORTH AND SOUTH AMERICA.—*Continued.*

	P. I. 1902	Ph. Brit. IV 1898 and B. P. C.	U. S. P. VIII 1905 and Spanish Edi- tion 1909	Ph. Mex. IV 1904	Ph. Fr. V 1908	Ph. Hisp. VII 1905	Ph. Venez. I 1898	Ph. Germ. IV 1900	Ph. Chili I 1886	Ph. Arg. I 1898
Acidum hydrocyanicum dilutum.....										
Requirement.....	2	2w/v	2	I	2	2		0	0	0
Aqua amygdalæ amara Requirement.....	0.10	0	0	(?)	0	0		0.1	0	0
Aqua laurocerasi.....				(?)				0		0
Requirement.....	0.10	0.1			0.1	0.10			0.05	
Aqua phenolata.....		0	0	0				0	0	0
Requirement.....	2				2	2				
Sodii arsenas Requirement.....	Cryst.	Anh.	Cryst.	Cryst.	Cryst.	Cryst.		0	Cryst.	Cryst.
Liquor potassii arsenitis Requirement.....	1	I	I	I	I	I		I	I	0
Syrupus ferri iodidi Requirement.....	5	10	5	I		5	0.6	5	2	0.5
Tinctura cantharidis Strength.....	10	1.25w/v	10w/v	10	10	10	10	10	10	10
Menstruum.....	A70	A.90	A95	A70	A70	A70	A80	A90	A80	A80
Tinctura iodi Strength.....	10	2.5w/v	7	10	10		10	10	10	8.33
Menstruum.....	A95	A90	A95	A95	A95		A90	A90	A90	A90
Tinctura lobeliae Strength.....	10	12.5w/v	10w/v	10	10		20	10	10	20
Menstruum.....	A70	A60	Dil. A	A70	A70	A70	A60	A70	A70	A60
Cocaine hydrochloridum Requirement.....	Anh.	Anh.	Anh.	Anh.	Anh.	Anh.	0	Anh.	0	Anh.
Unguentum hydragryi Strength.....	30	48	50	30	50	30	50	33	50	50
Requirement.....		33	25			50	12		25	25
Vinum antimonii Strength.....	0.4	0.457	0.4w/v	0.3	0	0.4				0.4



ary importance. The Spanish name is usually given precedence, and in Mexico and Venezuela Spanish titles appear to be used almost exclusively.

In conclusion it may be pointed out that the protocol adopted by the Brussels Conference has been proven to be reasonable in its requirements, the medicaments that are included, with few exceptions, are widely used, and the nomenclature proposed, while elastic, is sufficiently uniform to be easily recognized. The several provisions have been generally adopted by the pharmacopœias of continental Europe and it is to be hoped that they will be fully complied with in forthcoming revisions of the several American Pharmacopœias.

With the desirability of instituting international standards of strength and nomenclature generally recognized, with the practicability of their introduction fully demonstrated, and with the need for a world wide science of medicine fully established, it would surely be a reflection on the scientific spirit and the progressiveness of American people if these several provisions were not included in each of our national pharmacopœias.

It is to be hoped, therefore, that the countries represented in the congress, assembled in the Metropolis of the South American Continent, will lend their influence to the further development of international uniformity in name and strength of widely used medicines and that the provisions of the Brussels protocol will be embodied in the pharmacopœia of each American nation.

TABLE I.

Showing titles for Cocaine Hydrochloride, Solution of Potassium Arsenite, and Fluidextract of Ergot, proposed in Brussels Conference Protocol and those used in the several pharmacopœias.

COCAINE HYDROCHLORIDE.

- P. I.—Cocainum hydrochloricum.
- U.S.P.—Cocainæ hydrochloridum.
- Ph. Hisp.—Chlorurum cocainæ.
- Ph. Fr.—Cocainum chlorhydricum.
- Ph. Germ.—Cocainum hydrochloricum.
- Ph. Mex.—Clorhidrato de cocaína.
- Ph. Brit.—Cocainæ hydrochloridum.
- Ph. Arg.—Cocainum hydrochloratum.
- Ph. Venez.—
- Ph. Chili.—Cocainum hydrochloricum.

## SOLUTION OF POTASSIUM ARSENITE.

P. I.—Arsenicalis liquor Fowleri seu Liquor arsenicalis Fowleri seu Kalii arsenicosi liquor.

U.S.P.—Liquor potassii arsenitis.

Ph. Hisp.—Solutum arsenitis potassici.

Ph. Fr.—Solutio kalii arsenicosi.

Ph. Germ.—Liquor kalii arsenicosi.

Ph. Mex.—Solución arsenical de Fowler.

Ph. Brit.—Liquor arsenicalis.

Ph. Arg.—Liquor kalii arsenicosi.

Ph. Venez.—Arsenis potassicus aqua solutus.

Ph. Chili.—Liquor Fowleri.

## FLUIDEXTRACT OF ERGOT.

P. I.—Secalis cornuti extractum fluidum seu Extractum fluidum Secalis cornuti; Ergoti extractum fluidum seu Extractum fluidum Ergoti.

U.S.P.—Fluidextractum ergotæ.

Ph. Hisp.—Extractum aquosum secalis cornuti.

Ph. Fr.—Extractum ergoti fluidum.

Ph. Germ.—Extractum Secalis cornuti fluidum.

Ph. Mex.—Extracto fluido de cuernecillo de centeno.

Ph. Brit.—Extractum ergotæ liquidum.

Ph. Arg.—Extractum secalis cornuti fluidum.

Ph. Venez.—Extracto fluido de Cornezuelo de centeno.

Ph. Chili.—

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NOTES ON THE QUALITATIVE AND QUANTITATIVE  
ANALYSIS OF OINTMENTS AND SIMILAR  
PREPARATIONS.

BY C. BRAUBACH.

LABORATORY OF FRASER & CO., NEW YORK.

The qualitative and quantitative determination of the constituents of an ointment (cream) used for medicinal or cosmetic purposes is usually intrusted to the analyst for the purpose of ascertaining the formula and of duplicating the original. An investigation concerning the correctness of a published formula of such a specialty is rarely the purpose of the analysis. The problem given

in the first case is generally the easier one. Notwithstanding the difficulty encountered in detecting fat, oil, wax, etc., in a mixture and the frequent impossibility of their estimation, the analyst possessing sufficient pharmacognostic knowledge may be able to combine the analytical data found with his knowledge of the *materia medica* to obtain a satisfactory result in duplicating the original, if this was the purpose in view. A correct qualitative and approximately quantitative determination of the principal constituents, medicinal or cosmetic, which do not belong to the excipient, viz., alkaloids, salts, sulphur, glycerin, etc., can be expected however from the analysis. The consistence of the excipient, if it should prove to be a mixture the constituents of which have been found, can be reproduced if necessary by experiment when the iodine number, saponification number, melting point, specific gravity, etc., do not give any clue concerning the proportions.

Details in reference to the ointment to be analyzed, stating its use and effect, antiseptic, anæsthetic, for inflammatory conditions, etc., or if for cosmetic purpose, bleaching and whitening the complexion, massage, liver spots, etc., often give valuable information about the ingredients which might be expected as, for example, mercury bichloride, certain alkaloids, hydrogen peroxide, salicylic acid, camphor, etc. With this preliminary knowledge one is often able to readily detect the one or the other constituent. A careful study of any literature accompanying the ointment is also advised.

A systematic arrangement how to proceed with the analysis which can be used for all cases naturally can not be given and must be worked out after making some preliminary and qualitative tests.

The following procedure is suggested:

1. Physical examination: color, odor, consistence, taste.
2. Microscopic examination.
3. Preliminary tests.
4. Analysis, qualitative and quantitative.
5. If indicated, preparation of a duplicate and comparison with the original.

In order to ascertain if an ointment is easily absorbed by the skin, its melting properties and stickiness, a little of the ointment may be rubbed in on the back of the hand, at the same time certain odors might be noticeable as, for example, the odor of cacao butter.

**MICROSCOPIC EXAMINATION.**—Spread a small amount of the ointment, about the size of a match's head, on a slide, using the

edge of another slide to distribute it in a thin layer over the surface. Examine first with a magnification of about 250 then 500 diameters. Repeat this after drawing slide several times through a small flame to allow fat which might be present to melt. The presence of starch, powdered drugs, crystalline or amorphous bodies, fatty acid crystals, etc., can thus be readily detected.

**PRELIMINARY TESTS.**—Submit a sample of the ointment in a test tube for about half an hour to the warmth of a steam bath. Water and glycerin when present will separate from fat. Salts and mineral matter may settle down or be suspended in the melted fat, for instance, lead carbonate, zinc oxide, boric acid, etc.

Determine the solubility of the excipient in ether, chloroform, benzin, alcohol, etc. Any water present must be removed by drying before applying the solvent. Starch, powdered drugs, talcum and others can be so separated from a fat-base and weighed after completely removing base with the proper solvent.

Ointments containing fats or fatty oils will give a greasy stain on paper which does not disappear on heating or exposure to the air (difference from ointments having starch paste, mucilage of tragacanth, soap, etc., as basis).

**Reaction.**—A strongly alkaline reaction may be due to sodium or potassium carbonate (for example in massage cream to be used for reduction). In this case shake a sample of the ointment in a test tube with hot diluted hydrochloric acid to see if there is effervescence. Zinc carbonate or calcium carbonate are frequently found in cosmetic creams.

**Moisture** (water) including volatile substances (volatile oils). An accurately weighed sample of the ointment, one to two grammes, is heated in a flat platinum dish at a temperature of  $105^{\circ}$  until weight is approximately constant, weighing at half-hour intervals. Too long continued drying must be avoided as fats are liable to oxidize with increase of weight. In the presence of a considerable amount of water it is recommended to mix the ointment in a platinum dish with a weighed portion of washed and freshly ignited sea sand. Considerable water can be incorporated with a fat-excipient other than lanolin and eucerin by the addition of borax, potassium carbonate or alum.

**Ash.**—This is preferably done quantitatively in order to save a second ignition for the quantitative analysis. Two to three grammes of the sample, which should be free from incorporated water, are



used for this purpose. A residue remaining may be used for qualitative analysis.

QUALITATIVE ANALYSIS.—*Metals.*—Three to five grammes of the ointment are reduced to ash in a porcelain crucible and the residue tested for metals in the usual way. It is a precautionary rule not to use a platinum crucible as the presence of lead (lead plaster, etc.) might damage the crucible. Mercury and its salts and arsenic, if they are present are volatilized, as are also certain salts of zinc and lead, which are more or less volatile.

Reinsch's test for arsenic and mercury. About three grammes of the ointment are boiled gently for five minutes with 5 c.c. of concentrated hydrochloric acid and 5 c.c. of water, having immersed previously a piece of clean bright copper foil. If the copper foil, after a lapse of five minutes, still presents the same appearance as it had before, no arsenic or mercury can be present. Should the copper foil, however, show a steel-gray deposit or appear lustrous-like silver, arsenic or mercury are apparently present. The copper foil is removed, washed with water, dried with filter paper and cautiously heated in a perfectly dry narrow glass tube, open on both ends. The sublimate will collect on the cooler portion of the tube. Arsenic is converted into arsenous acid, its tetrahedral or octahedral crystals are apparent under the microscope. A sublimate of mercury will be found to consist of very small globules. The hydrochloric acid used in this test must be free from arsenic. Oxidizing agents, such as nitrates, will interfere with the reaction.

Another method to test for metals (except silver) and acids is as follows: Five grammes of the ointment are repeatedly shaken with hot diluted hydrochloric acid, filtered, after cooling, through a moistened filter and the filtrate tested. Part of the filtrate may be dried down on the water bath to see if anything be left behind.

ALKALOIDS AND NARCOTIC EXTRACTS.—*Alkaloids.*—A sufficient quantity of the material is vigorously shaken with hot very dilute sulphuric acid, allowed to cool and filtered through a filter moistened with water. A portion of the filtrate is examined with two or three of the general reagents for the alkaloids, such as solution of iodine, phosphomolybdic acid or Meyer's reagent. Should a turbidity or precipitate form, the presence of alkaloids is suspected. The acid, aqueous filtrate is slightly supersaturated in a separating funnel with ammonia and the ammoniacal liquid extracted by shaking with chloroform, the latter is allowed to separate, removed

as far as possible, and the extraction repeated with another portion of chloroform. The chloroformic solutions are collected in a beaker and exposed to a gentle heat on the water bath until the chloroform is completely volatilized. Morphine is only very slightly soluble in chloroform; it can be extracted with a mixture of equal volumes of ether and acetic ether. The alkaloid is identified by the usual method.

*Narcotic Extracts.*—In the presence of narcotic extracts or if several alkaloids are suspected, also when considerable organic matter soluble in the acidulated water is present, it is advisable to resort to Stas-Otto's method of separating the alkaloid.

*Mineral Oil, Paraffin, Vaseline, Ceresin.*—Five grammes of the ointment are heated with 25 c.c. concentrated sulphuric acid at a temperature of 160° for fifteen minutes. The residue is intimately mixed with about 500 c.c. water. Vegetable or animal fats and oils, resin and wax are carbonized, any mineral oil, paraffin, vaselin, etc., present will separate on the surface of the water.

Another method is based on their indifference to alkalies as they can not be saponified. A few grammes of the material (admixtures of water, starch, salts, etc., must be removed by drying and filtration) are saponified on the water bath in an Erlenmeyer flask, closed with a small funnel, with a 4 per cent. alcoholic potash solution, shaking frequently to assist saponification. The mineral oil, paraffin or vaselin will be found floating in drops in the clear liquid. In the presence of beeswax the saponification should be carried out for at least one hour.

*Substances Soluble in Alcohol.*—Certain constituents can be separated from an ointment base by extracting with hot alcohol, filtering when cool and evaporating the solvent. Small quantities of wax, fat, oil, vaselin, lanolin, etc., will be dissolved at the same time, but not sufficient to interfere with a fairly accurate estimation of the alcohol soluble constituent, provided the latter is present in not too small quantities. Fatty acids, however, are more readily soluble in alcohol than fats, oils, etc. This must be taken in consideration if, for example, stearic acid is found to be present. Substances soluble in alcohol and liable to be constituents of an ointment are: resin, turpentine, balsam of Peru, tar, castor oil, croton oil, etc. Glacial acetic acid in place of alcohol can be used with advantage as a solvent in some cases. After the alcohol or acetic acid has been driven off on the water bath, the material left behind usually can be recognized from its physical appearance.

*Soap*.—If an ointment is mixed in a separating funnel with about three times its volume of ether and shaken with water, the latter will take up the soap. On addition of diluted hydrochloric acid to the aqueous solution a turbidity and separation of the fatty acids will take place. Instead of mixing with ether the ointment may be agitated with hot water, filtered after standing for about one hour and acidulated with hydrochloric acid as before.

Soaps insoluble in water (oleates, lead plaster) are decomposed on shaking with hot diluted hydrochloric acid, the latter dissolving the metal.

**FREE FATTY ACIDS.**—*Stearic Acid*.—These can be detected by treating the ointment with alcohol, filtering and adding an alcoholic solution of lead acetate. A white precipitate indicates the presence of a fatty acid. Resin and soap, however, give a similar reaction. One can also resort to the following test<sup>1</sup> for stearic acid: Melt a small quantity of the material in a porcelain dish, stir up the melted substance for a few moments with ammonia water and allow to cool. Remove the solidified mass from the surface, or filter through a wetted filter and acidulate the liquid with hydrochloric acid, when stearic acid will be precipitated.

Stearic acid when heated with alkali carbonates on the water bath forms salts with effervescence, giving off  $\text{CO}_2$ .

Stearic acid has a high acid number, 200–210, its admixture with fats, oils and paraffin may be suspected on finding a high acid number, when colophony, which also has a high acid number, is absent.

*Resinous Substances*.—Colophony, turpentine, etc. (see under substances soluble in alcohol). The presence of colophony can be detected by the following method, which was originally given in a somewhat different form by Parry for the detection of colophony in shellac.<sup>2</sup> The colophony is isolated from the ointment by shaking a small amount of the latter with hot strong alcohol, separating the alcoholic solution after cooling by filtration and pouring the filtrate in water. The precipitate is collected on a filter, dried, triturated with petroleum ether and filtered. If no precipitate forms and the liquid has the appearance of an emulsion, it should be evaporated to dryness on the water bath and the recovered colophony triturated with petroleum ether as before. On shaking the filtrate with a very dilute copper acetate solution, the petroleum ether will be colored emerald green in the presence of colophony.

Another color reaction for colophony has been given by Sans,<sup>3</sup> as

follows: On slightly heating in a test tube one to two c.c. neutral methyl sulphate with a little colophony, a rose red color is obtained which changes to violet and disappears on further heating. Neutral ethyl sulphate may be used for methyl sulphate. Resin, having a melting point of  $90^{\circ}$  to  $130^{\circ}$  C., will increase the melting point when added to fats as in cerates. A very characteristic odor can be observed on blowing out the flame of a burning ointment containing an appreciable amount of resin.

*Detection of Certain Fats and Rosin by the Odor of Their Acids.*—About three grammes of the ointment are saponified with alcoholic potash solution and the alcohol evaporated on the water bath. The resulting soap is taken up with water and the aqueous solution acidulated with hydrochloric acid. Tallow gives the odor of mutton broth; colophony and various other fats and resins also yield characteristic odors.

*Beeswax.*—Should the odor fail to give a clue, the admixture of beeswax to an ointment may be suspected from the peculiar clouds formed in a solution in petroleum ether. Beeswax is only partially soluble in petroleum ether, whereas most of the fats, oils, paraffin, etc., are readily soluble in this solvent. It is important that water, volatile substances as carbolic acid, mineral constituents have been removed before applying this test. Resin, castor oil and other alcohol soluble substances must be removed by shaking the sample two to three times with hot alcohol, filtering off and drying the remaining excipient. If about 0.3 grammes of the so prepared ointment base are dissolved in 4 c.c. petroleum ether in a test tube at a temperature of about  $18^{\circ}$  C. it will be found in the presence of beeswax that clouds, consisting of very small needles, are suspended in the solvent. Compare with a solution of a little wax in petroleum ether. To examine these needles under the microscope it is best to mix a drop of olive oil on a slide with a little of the petroleum ether containing the needles in suspension before covering with cover glass. Unfiltered wax shows pollen under the microscope.

*Lanolin.*—Lanolin is only very slightly saponified by an aqueous solution of potassium hydroxide; it can be saponified, however, with an alcoholic solution of potassium hydroxide, though with difficulty, preferably under pressure. For its detection, provided it can be separated sufficiently from other admixtures (either by shaking out with chloroform or removing foreign substances by shaking with



water, alcohol, melting, filtering and drying), the cholesterin reaction can be resorted to. (See Hager's Handb. der Pharm. Praxis, vol. 2, page 276.)

*Glycerin.*—It may be detected by melting the ointment (see under preliminary tests) or shaking out with hot water, evaporating on the water bath, purifying if necessary by taking up residue with ether-alcohol (1 + 3) and driving off the solvent. It may be identified by its sweet taste. On igniting with potassium bisulphate the odor of acrolein will be noticed.

Denige's tests are also useful.<sup>4</sup> The glycerin is oxidized to dioxyacetone by boiling with bromine water on the water bath, the product so obtained gives beautiful color reactions with thymol, resorcin, codein and  $\beta$ -naphthol in the presence of concentrated sulphuric acid. The reaction takes place either at room temperature or on heating. Thymol produces a bordeaux red color changing to pink red, on diluting. Resorcin causes a blood red color changing to yellowish red or yellow on diluting with glacial acetic acid or sulphuric acid (spec. grav. 1.8). Codein gives a greenish blue and  $\beta$ -naphthol an emerald green color with green fluorescence. If a solution of salicylic acid and potassium bromide is heated with dioxyacetone for two minutes on the water bath, a violet color is obtained; the salicylic acid may be substituted by guaiacol, the color produced will be a deep blue. Dioxyacetone gives the hydrazine reaction with phenylhydrazine, acetic acid and sodium acetate, the crystals can be identified under the microscope. Equal volumes of dioxyacetone solution and Nessler's reagent or Fehling's solution produce on heating a precipitate of metallic mercury and cuprous oxide, respectively.

*Casein.*—Frequently used in skin creams, is insoluble in water, alcohol and ether. It is soluble in dilute caustic alkali or alkaline carbonates also in diluted hydrochloric acid, containing less than 0.1 per cent. of hydrochloric acid.<sup>5</sup> Casein consists of about 14 per cent. nitrogen.

*Borax and Boric Acid.*—About five grammes of the ointment are melted in a flask and shaken with 10 to 15 c.c. warm water, acidulated with hydrochloric acid. The liquid is filtered off from fat or insoluble material when cold and tested with turmeric paper and ammonia. A negative reaction shows the absence of either borax or boric acid which, when added to an ointment, are present in nearly all cases in a quantity of not less than 0.5 per cent. Boric

acid will give the reaction with turmeric paper when shaken out with hot water; borax will give the test on setting free the boric acid, using acidulated water for extraction.

QUANTITATIVE ANALYSIS.—*Metals and Their Salts*.—A simple and sufficiently accurate method to estimate certain metallic compounds, insoluble in fat-solvents, such as zinc oxide, carbonates of zinc, lead, calcium and bismuth subnitrate when mixed with a fat excipient and no other substances also insoluble in the solvent are present, is as follows: A thoroughly dried and weighed sample of the ointment is mixed in a beaker with the proper solvent (see preliminary tests), the mixture transferred to a dried and weighed filter and the latter with the remaining substance washed with the solvent until all fat is removed. The filter with contents is allowed to dry at 100 to 105° C. until its weight remains constant. In calculating the percentage of the material thus obtained, the loss on drying the ointment must of course be taken in consideration.

For method of estimating metallic mercury in mercurial ointment see U.S.P.

A procedure for the estimation of metals in organic substances has been given by Rothe.<sup>6</sup> It is based on the observation that organic compounds when digested for a sufficient time with a mixture of fuming nitric acid and concentrated sulphuric acid, and subsequent heating until vapors of sulphuric acid escape, are decomposed on further heating with fuming nitric acid into carbon dioxide and water. To the material, which should be free from water, is added in a flask 10 to 15 c.c. fuming nitric acid and 2 c.c. concentrated sulphuric acid for each gramme taken and the flask heated on a sand bath until a continuous generation of gas takes place, avoiding too high a temperature. Later on the temperature of the sand bath is increased to drive off the nitric acid and cause the sulphuric acid to develop vapors. To this end the flask is heated over the free flame, after the nitric acid has escaped, until the sulphuric acid boils briskly. After allowing to cool, 5 to 10 c.c. fuming nitric acid are added and the flask heated again on the sand bath to slight boiling until the liquid turns light, which will require from one-quarter to one-half hour. Finally the flask is heated once more over the free flame to a brisk boiling until heavy vapors of sulphuric acid are given off. If the liquid assumes a brown color the organic matter is not completely destroyed and the operation must be repeated by the addition of another 5 c.c. of fuming nitric acid until

the sulphuric acid does not turn dark on boiling. Since the comparatively large amount of free sulphuric acid present may be objectionable during the final procedure, it can be driven off for the most part over a Bunsen burner without loss of metal. The last traces of the oxides of nitrogen are removed by diluting the residue with water and heating to the boiling point for a short time. The further treatment of the residue, now free from organic matter, is dependent on its chemical composition.

*Alkaloids and Narcotic Extracts.*—A sufficient amount of the ointment, containing about 0.03 of the alkaloid, is subjected to Stas-Otto's method and the alkaloid so separated either weighed or titrated with standard acid using cochineal as indicator. The quantity of the alkaloid found, if due to a narcotic extract, will usually give an idea of the amount of the latter.

*Mineral Oil, Paraffin, Vaseline, Ceresin.*—In admixtures with saponifiable fat, oil, etc. One to two grammes of the material are saponified on the water bath with an excess of a 4 per cent. alcoholic solution of potassium hydroxide. For details (see qual. analysis under mineral oil). Any volatilized alcohol should be replaced to keep volume constant. After saponification the alcohol is driven off for the most part, the mixture transferred to a separating funnel, made up with water to about 80 c.c. and thoroughly shaken with 50 c.c. of ether. The latter will dissolve the hydrocarbon, the aqueous layer retaining the soap. If the separation of the ethereal solution does not occur readily, a few c.c. of alcohol may be added to break up any emulsion by giving the liquid a slight rotary movement. The aqueous solution is removed and the ether in separator agitated with 10 c.c. of water to which a few drops of caustic alkali have been added. This is run off, the ether shaken with water, the latter removed and the ethereal solution collected in a tared flask. The aqueous liquid is twice treated in separator with fresh ether as before, each time washing the ether and adding it to the first portion. After reclaiming the ether by distillation, the flask containing the hydrocarbon is heated at 100° C. for one hour and weighed. Beeswax and spermaceti yield on saponification myricyl and cetyl alcohol, respectively, which bodies are soluble more or less in ether. Cetyl alcohol can be separated from the hydrocarbon by treating the ether residue with strong alcohol, which will dissolve it, leaving the hydrocarbon behind.<sup>7</sup>

*Substances Soluble in Alcohol.*—Proceed as stated under quali-

tative analysis, using a weighed quantity of the ointment, shaking out twice with the solvent. Drive off the latter on the water bath, dry in steam oven and weigh.

*Soap*.—Soluble soap, for example castile soap, may be shaken out twice with hot water, filtered after cooling, the filtrate evaporated and the soap dried and weighed. Soaps insoluble in water, zinc stearate, lead plaster, etc., can be estimated with tolerable accuracy by quantitating the metal (see quantitative analysis under metals).

*Stearic Acid*.—In the absence of other free fatty acids and alcohol soluble material, stearic acid may be estimated when in admixture with oils by introducing a weighed sample into a flask, adding about 50 c.c. methyl alcohol and a few drops phenolphthalein. The flask is immersed in hot water, its contents thoroughly agitated and half normal caustic alkali added until after vigorous shaking the liquid retains a faint pink color. The alcoholic liquid is separated from the oil, the alcohol evaporated and the residue taken up with water. The aqueous solution is agitated with a little petroleum spirit to remove any oil or fat, then separated and the stearic acid precipitated by the addition of diluted sulphuric acid. On shaking with ether, separating the ethereal solution and evaporating to dryness, the remaining stearic acid can be weighed.

*Resinous Substances*.—Proceed as given under substances soluble in alcohol (qualitative analysis), using a weighed quantity of the ointment, shaking out twice with hot alcohol (20 + 10 c.c.), cool on ice, filter, evaporate filtrate, dry and weigh. A fair approximate estimation of colophony in admixtures with neutral fats or oils can be effected by mixing the ointment with a mixture of alcohol and ether and titrating with standard decinormal sodium hydroxide solution. Each c.c. of decinormal alkali represents 0.034 colophony, taking 165 as the average acid number of colophony. Free fatty acids (stearic acid) when present in quantity, will vitiate the results.<sup>9</sup> This method may be used for estimating the proportions of colophony in a mixture with linseed oil used as bird or fly lime.<sup>10</sup>

Acid resin, such as colophony, can be separated from the neutral fats by boiling the substance with a strong solution of sodium bicarbonate or borax. After cooling, the aqueous liquid is separated from the fat and the resin precipitated from its solution by adding hydrochloric acid.<sup>11</sup>

*Glycerin*.—It may be approximately estimated after separating the fatty acids (saponification of the ointment with alcoholic potash



and acidulating with hydrochloric acid), supersaturating the liquid with sodium carbonate, evaporating, extracting with ether-alcohol (1 + 3) and weighing the remaining glycerin after drying at 90–95° C.

*Borax and Boric Acid.*—Two to five grammes of the sample are rendered decidedly alkaline with sodium hydroxide in a platinum dish and heated on the water bath until free from water. The residue is carefully ignited, the ash taken up with 20 c.c. water and hydrochloric acid added drop by drop, until all is dissolved. The liquid is transferred to a 100 c.c. flask, 0.5 gramme of calcium chloride, a few drops of phenolphthalein and a 10 per cent. solution of caustic soda added until a permanent slight pink color is produced. Finally 25 c.c. of lime water are added and the volume made up to 100 c.c. The solution is well mixed and filtered through a dry filter. To 50 c.c. of the filtrate sufficient normal sulphuric acid is added until the pink color disappears, then methyl orange and the addition of the acid continued until the yellow is just changed to pink. A fifth normal solution of caustic soda is now added till the liquid assumes a yellow tinge, excess of soda to be avoided. The carbonic acid is expelled by boiling, the solution cooled, a little phenolphthalein and an equal volume of glycerin added and titrated with standard sodium hydroxide until a permanent pink color is obtained.<sup>12</sup> One c.c. of fifth normal soda solution represents 0.0124 grammes crystallized boric acid or 0.0191 grammes borax ( $10\text{H}_2\text{O}$ ). On titrating the boric acid 50 c.c. of glycerin should be present for each 0.1 gramme of the acid.

*Chemical Constants of Fats, Oils and Waxes.*—Refractive index, iodine number, acid number and saponification number. In some cases it is advisable to resort to the determination of one or several of these constants, for example, as a proof of the presence of a certain fat, indicated by physical appearance or qualitative test, and the absence of other fats or oils. For instance, an excipient is found to be lanolin from its appearance and the cholesterin reactions, yet the analyst may not be sure that no other fat, possibly lard or tallow, is also present, particularly when alcohol or water soluble admixtures have been separated previously from the fat bases and its physical character somewhat altered.

*Total Nitrogen.*—The determination of the nitrogen content is frequently indicated to either quantitate a constituent of the sample,

—casein, alkaloids, etc., or to show the absence of such bodies. A small nitrogen content, due to impurities in fats, oils or waxes, might, however, be met with.

*Melting Point.*—At least 24 hours should have elapsed since the last melting, as melted fats require a certain time to acquire their normal melting point. Products obtained by melting together beeswax, paraffin, stearic acid, etc., have a melting point lower than the mean of their constituents.<sup>13</sup> The presence of an appreciable amount of carnauba wax (melts at 84 to 86° C.) or rosin (90 to 130° C.) in a fat base increases the melting point. The sample must of course be free from water, salts, mineral matter, glycerin, etc.

*Ash.*—See under preliminary tests.

*Remarks.*—As a general rule water or alcohol soluble constituents are extracted by treating the sample with the hot solvent, concentrating the aqueous liquid or evaporating the alcohol, and testing in the usual way or identifying the residue from its physical character. The water and alcohol insoluble constituents are separated from a fat basis by dissolving out the fat with ether or chloroform, filtering off the solution and identifying the residue on filter either chemically or microscopically. In the presence of water soluble and water insoluble substances, for example, boric acid and zinc oxide, the former are removed as before; the remaining fat containing the water insoluble substance must be thoroughly dried before dissolving fat in solvent. Two water insoluble constituents of an ointment, for example, starch and zinc oxide, or starch and talcum, may be separated from each other after removing fat by using the proper solvent of one, viz., diluted acid for zinc oxide or incinerating starch, which will leave the talcum behind. Volatile substances as volatile oils, carbolic acid, etc., can be separated by distillation with live steam and their identification thus made easier. If a certain known odor of a volatile oil can not be identified by its name, the following method has been found practical but not very scientific. On looking over the index of the volatile oils in the dispensatory or other suitable pharmaceutical manual, one might strike suddenly the name of the oil in question or might be able to select a few for comparison with the original.

The amount of fat basis in an ointment can be estimated by dissolving a weighed sample, which must be free from water, in chloroform, making up to a certain volume and evaporating an ali-

quot part of the clear solution to dryness. Resin and other alcohol soluble substances, if present, are removed previously by shaking with this solvent.

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- <sup>4</sup> *Compt. rendues*, 148, 570-72.
- <sup>5</sup> Allen, Commercial Org. Anal., vol. 4, p. 100.
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- <sup>7</sup> Allen, Commercial Org. Anal., vol. 2, part 1, pp. 113, 114.
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- <sup>9</sup> *Ibid.*, vol. 2, part 3, p. 165.
- <sup>10</sup> *Ibid.*, vol. 2, part 3, p. 165.
- <sup>11</sup> *Ibid.*, vol. 2, part 3, p. 147.
- <sup>12</sup> Prov. Methods U. S. Dep. of Agriculture, Bulletin No. 65, p. 110.
- <sup>13</sup> Allen, Commercial Org. Anal., vol. 2, part 2, p. 145.

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## THE STATE CONTROL OF CONTAGIOUS AND INFECTIOUS DISEASES.\*

BY DR. SAMUEL G. DIXON,  
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"The State Control of Contagious and Infectious Diseases," the subject on which you have requested me to address you, embraces two ideas, first the general control or supervision of infections in every part of the state, whether civic or rural, and second their special, absolute control in the rural districts only.

The former relates to incorporated municipalities, cities, boroughs and townships of the first-class which are autonomous in regard to sanitary administration, the second to those quasi-municipalities known as townships, which includes also villages. In the former the State assumes no control unless municipal control should become so imperfect or careless as to render the conditions a menace to other populations, in the latter the state has absolute control, organizing the administration, formulating the regulations and appointing the officials and agents. It will be understood therefore that what I

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have to say will apply principally to the rural districts of the commonwealth.

PAST CONDITIONS.—Up to the year 1895 there had been no systematic law for the control of contagious and infectious diseases in this state. Every city and prominent borough had its own form of health government and formulated its own system of laws. In that year, however, representatives of several municipalities united with the former State Board of Health in drawing up a system of regulations for preventing the spread of such disease, which was enacted by the State Legislature and which was sufficiently comprehensive to entitle it to be denominated the "Pennsylvania Sanitary Code for the Restriction of Communicable Diseases." This at once became legally effective for every incorporated municipality in the State. But except in the case of a few townships in which the school boards availed themselves of their right to organize as boards of health the whole vast domain outside of city and borough limits was in a state of chaos so far as any regular control of such diseases was concerned.

MODERN LEGISLATION.—With the statesmanlike legislation of 1905, however, giving new powers and appropriating increased means to the health authorities, order sprang out of chaos, and a new condition of things came into being.

What was considered at that time a very liberal appropriation, three hundred thousand dollars, was given the department for the two years 1905 and 1906. So rapidly did the work grow, however, that in 1907 the Legislature appropriated to the department two million dollars. Six hundred thousand of this was specifically set aside for the establishing of the State Sanatoria for Tuberculosis and four hundred thousand for Dispensaries for Tuberculosis. Still the work continued to grow. The people gave it their hearty support and in 1909 the unprecedented appropriation of two million dollars for tuberculosis and one million dollars for general health work, was given the State Department of Health.

ORGANIZATION.—To-day the department is a well organized, fully equipped fighting force and its work along all lines of conserving public health, in which it has been engaged, has met with gratifying success.

Pennsylvania has an area of 44,985 square miles and contains 30 cities, 849 boroughs, 67 counties and 1547 townships, a total of 2426 separate and distinct municipalities, which to a certain extent



must be considered individually in all public health work. About three million of Pennsylvania's seven million population reside in rural districts. In cities, boroughs and in a few townships, namely those of the first class, provision has been made, as already said, by legislative enactment for the appointment of boards of health. Only by constant urging and untiring educational work, however, has the State Department of Health succeeded in getting many of these small boroughs to organize health boards. In over fifteen hundred townships absolutely no permanent health organization had been provided by law. This gives some idea of the broad field in which the state health authorities' work is found.

In each of sixty-six counties of the State the department has now a thoroughly trained medical inspector assisted by a corps of township health officers. There are altogether seven hundred of these health officers distributed throughout the state. To them the physicians report all cases of communicable diseases and the health officers promptly placard the premises and establish the necessary quarantine. Upon receiving notice from the physician of the termination of quarantine the health officer thoroughly disinfects the premises. As a proof of the results being obtained from educational work it has been gratifying to note the constantly increased number of requests from householders to have their homes disinfected after cases of tuberculosis.

These health officers for the past two years also have been making regular inspections of the sanitary conditions of all schools in the rural districts, and the result has been a very marked improvement of such schools.

MEDICAL INSPECTION OF SCHOOL CHILDREN.—The department is putting in operation a system of medical inspection of the school children in the rural districts. This inspection is being made by skilled physicians.

In view of the results already accomplished by medical inspection of schools in some of the larger cities and municipalities throughout the country, we are safe in saying that the standard of health of the children in the country schools in Pennsylvania will be raised materially by this work, and that the spread of contagious and infectious diseases will be greatly curtailed.

REPORTING OF CONTAGIOUS AND INFECTIOUS DISEASES.—One of the first steps taken by the department was to arrange for the reporting of all contagious diseases, as well as deaths from the same,

to the central office. At the same time it was felt that the list of diseases required by state law to be reported was extremely defective. The following additional diseases were therefore made returnable:

Anthrax, actinomycosis, glanders, trichiniasis, rabies, malarial fever, bubonic plague, measles, whooping-cough, tuberculosis, chickenpox, German measles, mumps, epidemic dysentery, tetanus, erysipelas, pneumonia, puerperal fever and trachoma.

This makes nearly thrice the number previously required to be reported by the laws of the state. In each case however, there was a reason which appeared to the department good and sufficient for requiring that the department should be made aware of its presence, and the next Legislature incorporated them all into the law.

An analysis of the specific character of each of the diseases which have been added to the report card will show that each and every one is justly entitled to be placed thereon, and that their importance is not to be denied.

Anthrax, actinomycosis, glanders, trichiniasis and rabies are all known to be communicable to man from the domestic animals and to be difficult of cure, often fatal.

Malarial fever can only be eradicated by screening every case from the *Anopheles Maculipennis* mosquito, while at the same time a vigorous warfare is waged against the insect itself. Bubonic plague is advancing upon us with no uncertain step and its mode of transmission is no longer a mystery. Every civilized country now makes tuberculosis reportable, while measles and whooping-cough, although scoffed at by the unthinking, cause each far more deaths than scarlet fever and smallpox combined.

During the week ending Feb. 28, 1910, among the deaths registered at the General Register Office, Somerset House, London, were 14 from measles, 4 from scarlet fever, 11 from diphtheria, 45 from whooping-cough, and 11 from diarrhoea, from smallpox 0 and from typhoid fever 0. During the three weeks previous the deaths from whooping-cough were 57, 61 and 53 respectively. Thus, during a week in which the deaths from whooping-cough were below the average, that deadly disease, so little regarded not only by the public but by the medical profession and even by the majority of boards of health, out of the victims of the nine most dangerous communicable diseases was responsible for the deaths of more than one-half.

DISINFECTION.—The control of contagious and infectious dis-

eases cannot be accomplished without the systematic and free use of disinfectants. This is recognized in all legislation on the subject. The Act of Assembly of April 14, 1903, however, took a step in advance in providing that all schools and colleges in cities in this state shall be disinfected at intervals not exceeding two weeks in accordance with a modern method and system of disinfection, such method and system to be approved by the local board of health if there be one, otherwise by the state health authorities.

Formaldehyde is a powerful disinfectant, and causes practically no injury to delicate fabrics or room furnishings and therefore is the principal disinfectant used by the state.

In using formaldehyde gas for disinfection, the air of the room should be both warm and moist. The latter condition may be effected by suspending wet sheets about the room.

An effective and economical method of generating this gas is by the addition of the official (U.S.P.) solution of formaldehyde to potassium permanganate.

Eight (8) ounces, by weight (one measure) of commercial potassium permanganate crystals is required for each pint of a solution of formaldehyde (at least  $37\frac{1}{2}$  per cent.) in disinfecting every 1000 cubic feet of air space.

Briefly, this method may be described as follows:

First: Secure a tin, agate-lined or iron pail with a flaring top which has a capacity at least equal to ten times the quantity of disinfectants to be used.

Second: Place the potassium permanganate crystals in the pail spreading them evenly over the bottom.

Third: Set the pail containing the crystals in a pan, metal wash tub or boiler containing water, a brick or stove lid being placed under the pail.

Fourth: Pour the formaldehyde solution from a dipper or some wide-mouthed vessel over the crystals of potassium permanganate.

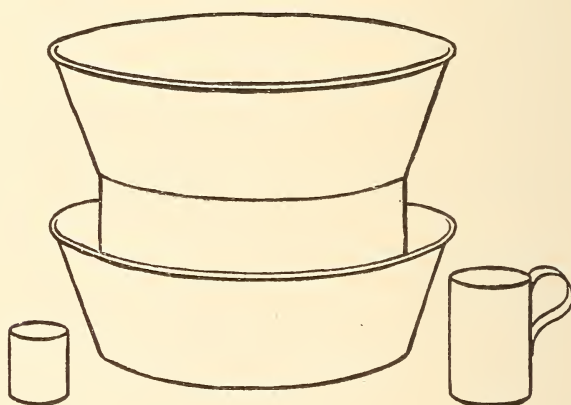
Fifth: Seal the door of exit including the key-hole and crevices about the door knob. This must be done quickly as 80 per cent. of gas is liberated during the first five minutes.

Sixth: Leave the room closed for six hours.

But observe this caution: It has been determined in the laboratories of the department that the gas so liberated is slightly inflammable. The room should be warm and moist, but under no circumstances should the chemicals be mixed and this form of disinfection

performed in the presence of a live fire or flame in the room. A separate container should be used for every pint of formaldehyde solution and proportionate amount of potassium permanganate required. It would be well to surround the vessel within which the container is placed, for a distance of at least three feet, with some absorptive material to receive any stray bubbles, thereby protecting the floor from any possibility of resulting stains.

This cut shows the Pennsylvania State Department of Health's modification of the vessel designed by the Maine State Board of Health for use in liberating formaldehyde gas from a water solution, by means of potassium permanganate.



Vessel for use in liberating formaldehyde gas from a water solution, by means of potassium permanganate. The larger funnel-shaped container measures 15 inches diameter at the top; 11 inches at the bottom, the inside depth or height of the flaring part 5 inches, and the depth or height of the lower part 6 inches. The pan measures 15 inches diameter at the top, 11 inches at the bottom and has a straight height or depth of 5 inches. The dimensions of the vessel have been fixed by empirical trial as ample for the diffusion of the gas, reducing the danger from ignition when in contact with a live flame to a minimum. The pan within which water is placed interlocks with the container proper, leaving sufficient space between the vessels for the circulation of water which protects the floor from heat generated by the chemical action. For convenience in carrying, the pan is made to nest in the top of the container proper. Three pints of liquid formaldehyde and twenty-four ounces of potassium permanganate may be safely used in this vessel without danger of overflow.

A cardinal point in disinfection is to attack the germ at the earliest possible moment after its escape from the body. Especially in all water-borne diseases, "Death in the bedpan" should be our slogan. And this leads me to call attention to the discovery in our laboratories of the presence of the germs of tuberculosis in sewage which will make it necessary to place that disease in the water-borne category, as a reasonable possibility.

PROPHYLAXIS.—Among prophylactics vaccination for smallpox is of course *facile princeps*.



So far from relaxing our legal requirements in regard to this measure we must constantly and combinedly aim to reach the German standard. When this is reached all over the world, Jenner's prophesy will be realized and smallpox will be banished from the earth.

Diphtheria antitoxin is a close second. Then follow the various serums and so-called vaccines, including the anti-rabic virus.

For the mosquito-borne diseases, destruction of mosquito-breeding areas, mechanical screening, destruction of mosquitoes in houses by the employment of fumes of narcotic plants.

For water-borne diseases filtration both of water and sewage with the addition of disinfectants in some exceptional cases.

The only drugs to which the name of specific can be applied are mercury in syphilis and quinine in malaria; but many of the serums are both prophylactic and specific, while certain of them have as yet only proven to be specifics.

The circulars of the department for the management of the various contagious diseases contain full instructions for the proper use of disinfectants as required in the case of each disease.

The Department of Health, therefore, urges upon all school directors, trustees, principals and presidents of schools and colleges outside of cities in this state the importance of protecting the health of their pupils and students, and of the entire community as well, by prompt and regular attention to this duty.

As the law provides no fixed period for rural schools, the Department of Health recommends that the desks, wood work, shelves and floors of school rooms, in addition to the customary scrubbing with soap or lye, be wiped at the end of each week with a cloth saturated with a 4 per cent. solution of liquor formaldehydi (U.S.P.).

Slates and slate pencils, if used, should be wiped off with the same. Sunlight and fresh air should be freely admitted.

At the end of each month, disinfection with formaldehyde gas should be practised.

DAIRY INSPECTION.—The communication of typhoid fever, scarlet fever and diphtheria through the medium of infected milk is a thoroughly well recognized fact. Hence it became necessary to go to the root of the evil and institute a system of careful dairy inspection by state officers.

Every community of any size in the State avails itself of the law to prevent the sale of impure or adulterated milk, but it is left to the

State Department of Health to guard the centres where the milk is produced. Therefore, our township health officers are regularly instructed to inspect the dairy farms in Pennsylvania. The total number of dairies inspected in 1908 was 17,618. Of these 2,442 were found to be in a condition which entitled them to the highest commendation. Of the remainder many were comparatively clean and carefully conducted but failed in one or more of the eight particulars noted on the inspection card.

For instance, on 480 farms, cattle were found to be drinking polluted water. In about 2500 dairies, the floors of the stables were in an extremely filthy condition. In about the same number the milkers did not wash their hands or the udders of the cows before milking, nor did they wear any clean protective covering to prevent dust and filth from their clothing falling in the milk.

It has been gratifying to discover that so far from appearing antagonistic the dairymen have been generally most ready to co-operate with the agents of the department in the inspections and to afford every facility, appreciating that it was to their interest to comply with all the instructions furnished by us and thus secure the confidence of the public in the purity of their product.

STREAM INSPECTION.—Side by side with the work of general medical inspection, has gone the campaign for pure water. This has been conducted by a fully equipped sanitary engineering division. To stop the pollutions of the waters of the state and reclaim them as nearly as possible to their virgin purity—this is a work fraught with obstacles and yet so important to the health of our people that it invites our most earnest efforts.

Five years ago the picture of stream pollution in Pennsylvania presented a sorry sight; the individual householder constructing an overhanging privy and polluting the stream that finds its way past his property; the small town defiling with raw sewage a stream of water that is expected to quench the thirst of villagers not far away; the large municipalities discharging the contents of their extensive sewers into the river that is the water supply for thousands and thousands of human beings down stream. This had been going on for generations.

Since the organization of our Sanitary Engineering Division, 18,945 private sources of stream pollution have been abated upon notice from the department, not to speak of the thousands more that have been stopped through the moral influence of this work.

Sixty-seven modern sewerage disposal plants have been either built or are in the progress of construction as approved by the state. Two hundred and five other municipalities and private sewerage corporations are preparing to submit plans for sewage treatment, for only on condition of their so doing have they been permitted to extend their sewerage systems. Already thirty-five modern water filtration plants have been approved by the state and are either built or being erected.

The people are beginning to appreciate that sanitary methods of sewage disposal and water purification are not costly compared with the money outlay that typhoid fever demands of our State every year, not to speak of the awful harvest of misery, suffering and death that it reaps.

In view of the work that has thus been done in cleaning up the streams of Pennsylvania, it is encouraging to note that 1908 showed a decrease of 1088 deaths from typhoid, compared with 1907, in which year there were also fewer deaths by 379 than in 1906. This is in the face of a rapidly increasing population, so that the actual decrease in point of numbers does not represent the full saving in lives.

DISTRIBUTION OF DIPHTHERIA ANTITOXIN.—I know of no work that the department has done which has been more gratifying to me personally than the saving of lives of little children by the free distribution of diphtheria antitoxin among the poor of Pennsylvania.

Since October, 1905, the Health Department has distributed 49,443 packages of antitoxin. It has treated 19,929 sick people, mostly children, who, but for the state's intervention, would have been neglected. In the old days about 10,000 of these children would have died; as a matter of fact, only 1725 died. Nearly all those who died were children who did not receive the antitoxin until the late stages of the disease. The detailed statistics of the department show that the earlier the sick child receives the antitoxin, the greater his chances of recovery. These facts should emphasize the pressing need, in all cases, not only of antitoxin treatment, but of this treatment at the earliest possible time. The department has also thoroughly tested the powers of antitoxin as an immunizing agent. Diphtheria, as every one knows, is one of the most virulently contagious diseases. It travels like lightning from the sick to the well. In the crowded homes of the poor, many of them ideal culture tubes for the growth of the microbes, its virulence is especially marked.

The department in three years has immunized with antitoxin 14,527 persons, nearly all children, who had been exposed to the disease. Of these only 251 acquired it—a little more than one per cent. The State Department of Health's free distribution of antitoxin to the poor, therefore, has saved over 8000 lives at an average cost of seven dollars each and prevented contagion in several thousands of cases at an average cost of two dollars.

I cannot too earnestly acknowledge the cordial manner in which my colleagues of the medical profession have supported me in my efforts for the control of infection. At great personal inconvenience they have performed the not inconsiderable labor of reporting contagious diseases and it is gratifying to be able to state that the more intelligent and careful physicians are now setting a good example to their less scrupulous professional colleagues by using protective gowns in making examinations in cases of communicable disease and disinfecting their persons and especially their clinical thermometers, and, in the same way, doctors of dental surgery are cleansing and disinfecting their instruments and the separate handles of the same after use in each case.

To you, gentlemen of the pharmaceutical profession, do we owe acknowledgments also for your readiness to act, entirely without compensation, as distributors of antitoxin, thus enabling the department to reach every poor sufferer in the state with the promptness which is so essential to the successful use of that agent.

CONTROL OF TUBERCULOSIS.—As has already been stated the Legislature of 1907 gave the State Department of Health a total appropriation for tuberculosis of one million dollars and in 1909 increased this appropriation to two million dollars.

The present plan of the state governmental anti-tuberculosis work may be summarized under the following headings:

First: The collection and tabulation of statistics relating to tuberculosis through official morbidity and mortality reports of each individual case.

Second: The establishment of one or more sanatoria for the treatment of incipient cases, including infirmaries for advanced and hopeless cases.

Third: The establishment of dispensaries in each county of the state for the care of cases which cannot avail themselves of sanatorium treatment, including home visitations and the study of occupational conditions.



Fourth: The maintenance of pathological laboratories for the free examination of sputum and tuberculous lesions and biological laboratories for the possible development of immunitive and curative products.

Fifth: The restriction of tuberculosis by the disinfection of rooms, buildings (private and public), conveyances and carriers, and by supervision and regulation over the general avenues of infection.

Sixth: The dissemination of knowledge relative to the communicability, care and prevention of tuberculosis.

The collection and tabulation of statistics relating to tuberculosis is the first essential work in the campaign against this disease as it is in the war against all communicable diseases. The law of the commonwealth now requires that a physician shall report to the health authorities each and every case of tuberculosis occurring in his practice.

Up to December 31, 1909, 2365 patients had been admitted to the Pennsylvania State South Mountain Sanatorium near Mont Alto. The present capacity is 720. This Spring, ground has been broken by the Department of Health for a second sanatorium on the beautiful tract of land at Cresson, which Andrew Carnegie so generously gave the commonwealth for that purpose.

It is also a pleasure to be able to announce that Mrs. B. F. Jones, of Pittsburg, has expressed her interest in the sanatorium scheme by offering the department a commodious dwelling house and lot close by the tract given by Mr. Carnegie. This will enable us to commence the reception of patients at Cresson during the present Summer without waiting for the completion of the larger buildings.

Ground has also been purchased for the erection of a sanatorium at Hamburg among the beautiful hills of Berks County, which will be easy of access for the teeming populations of Philadelphia and the eastern counties.

TUBERCULOSIS DISPENSARIES.—Pennsylvania leads the entire country in the number of dispensaries it has established for the treatment of tuberculosis. One hundred and fourteen of these dispensaries have already been established at as many points in the state. Up to December, 1909, 21,227 poor tuberculous sufferers had received medical aid and the attention of trained nurses which these dispensaries provide.

Each dispensary is in charge of a chief physician, from one to

thirteen assistants, and one to five nurses according to the number of patients under treatment, and is open at convenient hours, day or evening, to accommodate the occupational demands of those who are able or who are compelled to work. The location has been determined with a view of reaching the most populous centres. The great object of the dispensary is to reach each individual case of tuberculosis and by competent medical advice, treatment and supervision ameliorate or entirely relieve the physical condition and at the same time to educate the people as to the communicable character of this disease, to the end that others may not become infected through ignorance or carelessness. The dispensary nurses are required to make visits to the homes of dispensary patients and advise as to the methods of personal hygiene and home sanitation; instruct non-infected persons of the household as to the dangers, and how to avoid infection; to spread the doctrine of fresh air, sunlight, rest, proper foods, temperate habits, and compliance with the instructions of the medical advisers; and at the same time to discover unsuspected cases.

In all the larger dispensaries the "class system" has been inaugurated. Under this system classes are organized among the patients, each of which contains not over twenty-five members. The number of classes varies, being governed by the needs of the individual dispensary. The classes meet at regular intervals, some weekly, but usually every two weeks. The members are instructed to take and record their own temperature, pulse and respiration. This they do as frequently as the class leader may direct. Not only do the patients record these particulars, but they are also instructed to make careful notes of their condition, feelings and actions. Memorandum books are supplied for this purpose.

At the class meetings patients are encouraged to converse among themselves and compare notes as to their experience. The note books are submitted to the inspection of the class leader, who carefully reviews each one. Faults are pointed out, and misfortunes discussed with a view of avoiding their repetition and minimizing unfavorable consequences. Often the ingenuity of one patient will be of great assistance in solving the difficult problems of another. Patients are weighed and the result commented upon.

Indigent dispensary patients are supplied with nitrogenous food-stuffs in the shape of milk and eggs. In addition to food supplies the dispensaries furnish liberal quantities of paper napkins and

bags, pressed paper sputum cups for use in tin forms and pocket cuspidors.

Earnest effort is made through the dispensaries to educate the people in each community to a sense of the value of thorough room disinfection. The Department's Health Officers are instructed in the work of disinfection and supplied with the necessary equipment. A postal card sent to any health officer will secure his speedy attention. Not only the dispensary physicians, but every practitioner in Pennsylvania, is supplied with a list of the names and addresses of the health officers located in his own and adjoining counties.

The following, translated from the Report of Prof. F. Egger, the delegate from the Federal Council of Switzerland to the recent International Congress on Tuberculosis at Washington, is of interest as showing the impression made on an intelligent and cultivated foreign expert, by the part which our state is taking in the great world movement for the control of tuberculosis. Professor Egger says "Instructive as it would be to become acquainted with the excellent regulations of the States of Maryland, Massachusetts and others, we must content ourselves with sketching the measures adopted by the State of Pennsylvania, partly as we observed them personally and partly as they were presented in an admirable collective exhibit accompanied by a catalog full of reliable information at Washington." After giving quite a full account both of the Mount Alto Sanatorium and the Dispensaries, he says:

"If I have taken pains to depict the noble undertakings of America in the field of the contest against tuberculosis this has been done not only in candid admiration and recognition of their achievements but also with the object of showing our country what energy and self-sacrificing public spirit can accomplish."

If you have followed me in this somewhat prosy discourse you will have noted that the policy of the department in attempting the control of contagious and infectious diseases has been to lay the axe at the root of the tree, to embrace all, not only a few, communicable diseases, to insist on receiving information of every case, to make isolation and quarantine real and not perfunctory, although carefully modified as the nature of each disease may permit, to make disinfection thorough and complete, performed with real germicides, not simply bad smelling deodorants, and to use them where they will do the most good, to keep disease-breeding organisms out of our water and out of our milk as well as out of our air, to educate

our people to the cardinal virtue of cleanliness, and to lead the ignorant and disaffected to appreciate that the state government, so far from desiring to oppress them, is their best friend, ever ready to protect, advise and help them in their illness and misfortunes.

Convinced of the cardinal truth that the greatest defence against tuberculosis is a sturdy, vigorous human system which in turn can only be built up by an adequate supply of wholesome nourishing food, it undertakes to instruct the mothers of families in the selection of foodstuffs so that the greatest amount of nutriment may be procured for the least expenditure of money, and how the food may be cooked in such a way as to be most easily digested and have its nutritious properties most thoroughly conserved.

Thus through the physician and the nurse the state government comes very near to the unfortunate consumptive. Instead of being a cold and heartless abstraction, relentlessly working out its function of ruling, regardless of the suffering which may follow, it enters in a very real way into his life.

Heretofore, misled by the propaganda of the foreign anarchist, he has regarded the state with jealous suspicion as his natural enemy, whose principal object is to impose upon him oppressive laws and regulations, interfering with his personal liberty and taking his little all in exorbitant taxes. Now, to his surprise, he wakes up to find in his hour of trouble that the government is his thoughtful friend, ready to instruct him in better ways of living, how to get good wholesome food, and how to make his money go as far as possible in buying it, nay even when sickness has robbed him of his hard earned store, ready to furnish him the food best suited to restore him again to health and usefulness. It will be strange indeed if such treatment does not take the kinks out of his warped and twisted consciousness and lead him to become, instead of an anarchist, a friend and supporter of the state.



## THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.

BY EDGAR F. HEFFNER, Secretary.

It affords me a great deal of pleasure to have the honor of talking on the work and objects of our Association in this College, which has contributed more than any other institution toward the success of our state organization by furnishing many of the active workers, who have used the knowledge and training received here to aid in improving drug conditions, and to place the Pennsylvania Pharmaceutical Association in first place in the ranks of the state organizations.

The efficiency of our organization and the high character of the original material secured each year by our efficient chairman of the Committee on Papers and Queries, Professor LaWall, have time and time again brought forth strong commendations from the Pharmaceutical Press, which should be very gratifying to our members.

In point of actual dues-paying membership the Pennsylvania Association also leads, as we have nearly 1000 members who are in good standing, but in the number attending the meetings each year we are lamentably low, and are being put to shame by associations having half our membership. It is a crying shame that the work of our Association is only appreciated by one out of ten members to the point of his attending the meetings, and many think that the policy of holding the meetings at summer resorts each year for the past ten years is to blame and has been responsible for the low attendance.

So I am here to-day as an advance guard of an "On to Philadelphia" movement for 1911, and to endeavor to enlist your aid in making this year's meeting the largest and best meeting we have yet held.

Measures of vital importance to every retail druggist will be before our meeting, and in order that these measures may most nearly represent the sentiment of the best of our Association it is very essential that you attend the meeting and get as many of your friends and neighbors to go as you can.

It would be quite a relief to the officers and committee-men to have the "Anvil Chorus," who as a rule do not attend the meetings, make a change and come to our meeting this year. The

chances are that they would appreciate more the spirit that enters into our work, and become boosters instead of knockers.

Mr. Apple's paper in our Proceedings for last year impressed me greatly as being in part a solution of our difficulty in getting members to attend. In his paper he strongly urged the advisability of meeting next year at Philadelphia.

It is a fact that nearly 400 of our members are located in this city and probably 200 more within a convenient distance, over half of whom would attend the meetings. More of our inland members would attend a meeting here than at a summer resort, as it would give them a chance to purchase stock, and besides a large city at any time of the year appeals more to us "country fellows" and our wives. So for the good of the cause I ask you to attend this year's meeting and boom Philadelphia as a meeting place for 1911.

Our Executive Committee have during the past week sent out a circular letter to each retail druggist in the State setting forth strongly the advantage and reasons why they should become members.

This work has been supplemented by a letter to each member sent out by Mr. William E. Lee, chairman of the Membership Committee, asking each one to do his share toward securing the applications of those they know who are not now members. These appeals should certainly produce good results and will if you make a personal application of them and get busy.

Practically all of the laws regulating pharmacy in this State have been secured by or with the direction and assistance of our Association and are mile posts on the road of our progress toward our ultimate goal, "The restriction of the dispensing and sale of medicine to regularly educated Druggists and Pharmacists."

As a further step in that direction a draft of a law modelled after the New York and Ohio laws will be submitted to our Legislative Committee for consideration and approval in time to be presented to this year's meeting.

There is a considerable demand in the interior of our State for a law restricting the sale of medicines by grocers and peddlers. The unjust competition of these unqualified persons is an injustice to the pharmacist, who has spent at least four years to qualify himself and who is held to strict account for what he sells, while these people sell poisons and dangerous drugs with impunity and no regard for the law.

Any wholesaler doing a country-store business will tell you that more laudanum is sold by country grocery stores than by drug stores, and it is as a rule sold indiscriminately without any attempt to comply with the law.

This proposed law will restrict the sale of medicines (except proprietaries) in all cities of the first, second or third class, to registered pharmacists, provide for the registration of all country stores desiring to sell medicines in original packages, and will prohibit the issuing of a certificate to any store situated within one mile of a properly manned drug store. It will also place a prohibitive yearly license of \$240 on all wagon and house-to-house medicine peddlers, street hawkers, etc.

We will never have a more favorable time to push a law of this kind, as the present cocaine agitation and the unusually receptive condition of the public toward restricting the sale of drugs which has resulted, can be used to good advantage.

It is probable that the State Pharmaceutical Examining Board will ask our Association to endorse an amendment to the present Cocaine Law making the penalty more severe and providing for an appropriation large enough to vigorously enforce the act all over the State. As you are well aware the present campaign against the cocaine evil in this city will about exhaust the financial resources of the Board, and the State should certainly make ample provision for the enforcement of laws for the public good instead of compelling the Board to use the examination fees collected from applicants for registration, which should be used only for enforcing the present pharmacy and registration laws.

At the last meeting of the State Association a committee was elected, with ex-President Walton as chairman, to draft a model Anti-Narcotic Law, and submit it to the Association for approval at this year's meeting. This Committee at the present time are awaiting the action of Congress, two bills of a similar nature having been introduced but not acted on up to this time.

It is my personal opinion that independent of the action of Congress this Association should endeavor to obtain a law placing stringent restrictions on the sale of morphine, codeine, and preparations containing these alkaloids in quantities sufficient to enable them to be used as a narcotic.

The evils resulting from the present careless sale of these narcotics are more widespread and vastly more terrible than the evils

resulting from the use of cocaine, as there are 100 victims of these drugs to one of cocaine.

Cocaine habitues are only found in isolated spots, mostly in the larger cities, whereas every little village or town is daily adding to the large army of those who are "Walking in the valley of the shadow of Death" by way of the opium route.

In our city, which I find no worse than other cities in the State, there are no users of cocaine at all, but over twenty-five regular users of morphine and opium, and in our county, containing about 25,000 people, I could not find one case of cocaine habit but found 100 would be a low estimate of the number of regular users of narcotic drugs.

I do not think the proportion in the larger cities is any less, so in your city alone it would be safe to estimate that there are over 8000 victims of the morphine habit and in the State more than 25,000.

Students of the social problem claim that a large proportion of prostitutes are victims of narcotic drugs, and there is no doubt but that a great many have fallen from respectable womanhood to the lowest depths through the use of morphine and opium.

Our Association should go on record not only as favoring such a law, but as using every means to secure a Law which will limit the use of these dangerous drugs to legitimate purposes.

A better and fairer law can be drawn by our Association than by persons knowing nothing of the actual conditions, and as a law will be passed eventually it would be only a matter of business wisdom for us to lead instead of being whipped into line.

What this may mean to us can be shown by a single example. The insistence of President Wallace as chairman of the Legislative Committee on the insertion in the Drugs Law of the Label exemption clause, and the declaration only (not percentage) of the presence of the specified drugs saved every druggist in the State the immediate expenditure of from \$10 to \$25 for new labels, and also from the danger of violating the law in not giving exact percentages which in some cases would be hard to figure out.

In conclusion I extend to you all on behalf of the State Association a cordial invitation to come to Buena Vista on June 28, 29 and 30. You will enjoy your vacation in Pennsylvania's most beautiful and delightful mountain region at a time of the year when all nature is at her best, and in addition your presence and interest will aid in the work for the advancement of Pennsylvania pharmacy.



## CORRESPONDENCE.

### A CORRECTION.

TO THE EDITOR AMERICAN JOURNAL OF PHARMACY:

Please note that there is a typographical error in the last issue of your JOURNAL. Instead of "sodium arsenate," on page 204, line 35, it should read "sodium arsenite."

Very truly yours,

May 14, 1910.

ELIAS ELVOVE.

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## BOOK REVIEWS.

THEORIE DER GEWINNUNG UND TRENNUNG DES ÄTHERISCHEN ÖLE DURCH DESTILLATION. (Grundzüge einer allgemeine Destillationslehre) von C. von Rechenberg. Mit zahlreichen Abbildungen und Tabellen. Bearbeitet im Auftrage der Firma Schimmel & Co. in Miltitz bei Leipzig. Selbstverlag von Schimmel & Co. Miltitz bei Leipzig. (Für den Buchhandel: L. Staackmann, Leipzig), 1900.

The present work is a comprehensive presentation of the theoretical principles involved in the distillation of ethereal oils and the separation of the various constituents through this process. It may in addition be regarded as a handbook on the fundamental principles of distillation and furnishes besides a valuable contribution to phyto-chemistry as well as applied chemistry. In the preface it is gratifying to note also that the second edition of the work on "Ethereal Oils," by Gildemeister and Hoffmann, is being prepared by Dr. E. Gildemeister and that this will cover two volumes, the first volume of which will probably be published before the end of the present year.

There is probably no other class of substances employed in medicines and in the arts which are so extensively used, and which at the same time are commercially of such varying quality and of which the users have so little knowledge, generally speaking, as the essential oils. We are greatly indebted to the firm of Schimmel & Co. for their pains in supplying valuable and authentic information for the benefit of the trade, as well as assistance of chemists; and for their generous employment of scientific members of their staff and also special chemists in correlating the results obtained in the

routine manufacture of essential oils on a large scale as well as for their special scientific investigations on new essential oils. The example thus furnished is one that may well be emulated, as already stated in a previous reference to the publications of this firm (*JOURNAL*, vol. 76, 1904, p. 214), for after all the manufacturer of medicines and like products must be guided by the same ideals as to the purity and efficiency of his products and in the discovery of new and valuable substances, as the practitioners of medicine and the teachers in medicine and pharmacy, if the practice and the theory are to go hand in hand. In other words, the manufacturer of medicines and pharmaceutical products can no longer afford to think alone of the commercial gains on his products, but must at the same time be imbued with a motive similar to that which impels the teachers and practitioners in the professions named to devote their lives to their chosen work with but secondary concern as to the pecuniary rewards.

The present volume, which is by von Rechenberg, might well be employed as a text-book by organic chemists, as it treats of the scientific principles involved in distillation processes in a manner which is illuminating and indeed inspiring. That this is not overstated is seen in the mere mention of the contents of the fourteen chapters of which the book is comprised: (1) Practice of distillation, involving a study of the action of steam in plant and oil distillation; (2) Dalton's law of diffusion; (3) distillation of mixtures of insoluble fluids; (4) distillation under reduced or increased pressure; (5) distillation at high temperatures; (6) the chemical-physical changes preceding and incident to plant-distillation; (7) special examples of distillation, as of lavender flowers in Southern France, the distillation of herbs in Spain, cajuput distillation in Ceram, cassia leaves in Southern China, the distillation of coniferous plants in Switzerland, the distillation of cananga flowers in Java, of rose petals in Bulgaria and linaloe wood in Mexico; (8) the influence of molecular association and dissociation in the process of distillation; (9) the influence of higher temperatures with and without pressure upon individual substances; (10) a chapter in general upon solutions; (11) the distillation of mixtures bordering on more or less soluble constituents; (12) the distillation of homogeneous mixtures at temperatures less than the boiling point; (13) the distillation of homogeneous mixtures not having a constant boiling point; (14) the distillation of labile addition compounds, and the distillation of homogeneous mixtures with maximum boiling points. H. K.

## PHILADELPHIA COLLEGE OF PHARMACY.

### SPECIAL LECTURES, 1909-1910.

MODERN METHODS OF FOOD MANUFACTURE was the subject of the ninth lecture of the series. The lecture was delivered on Friday, February 11, at 3.30 P.M., by Mr. L. S. Dow, of the Heinz Preserving Co., Pittsburg, Pa., and was illustrated by means of lantern slides. Prof. Samuel P. Sadtler, in introducing the speaker remarked upon the special interest of this topic to the food analyst and also on the interest which the public is beginning to manifest in the subject of pure and wholesome foods.

The lecturer dwelt more especially on the practice of food preserving. He enumerated the various methods and agents used in the preserving art, tracing their use in some cases back to pre-historic times. In discussing the older and newer theories regarding putrefactive and fermentative changes in food products, he spoke in part as follows:

"Modern food preserving in its broader adaptation may be said to have had its origin in the discovery by the Frenchman, Appert, in 1804, that an article of food first heated, then hermetically sealed and sterilized, would keep practically as long as the seal was intact, without the use of chemical assistance.

"In Appert's time and indeed, until recent years, it was generally thought that the things essential to the preservation of food in this manner were the exclusion of air and the application of gentle heat to cause a fusion of the principal constituents and ferments, in such a manner that the power of the ferments would be destroyed.

"One year later, de Heine, then in England, patented a process by which he claimed that food could be preserved by completely exhausting the air with an air pump. All attempts at this, however, seem to have been unsuccessful, until a process patented by Wertheimer in 1839 came to be used. This provided that the food to be preserved should be placed in tin or metal cans, the interstices being filled with water, juices or other fluid, and the lid securely sealed. The cans were then set in water and boiled, the air being expelled through small holes pierced in the lids. When the food was sufficiently cooked and the air entirely driven out, the holes were filled with solder, completing the process. Food thus treated would remain in a perfect state almost indefinitely. No very great improve-

ment has since been made upon that method and no change at all in the principle. And, while the theory of these men differed from that accepted by modern science, the same means were used and the same results obtained as to-day; the process here described being used in all large canning factories in America, as well as the countries abroad, and in principle at least, practised in every household in which fruits and vegetables are preserved.

"It is through the investigations of later scientists however—particularly, of Pasteur—that the food preserver has been shown that it is not the oxygen of the air which causes fermentation and putrefaction, but bacteria and other microscopic organisms."

The subject of food adulteration received a share of attention and that of chemical preservatives was considered at some length. With regard to the latter, Mr. Dow said, "The first objection to their use, and I believe the most glaring abuse that exists to-day, lies in their employment for the purpose of preserving partly spoiled and ill-cared-for vegetables and fruits." He claimed that every product of fruits and vegetables with which he was familiar could be successfully made in a commercial way without artificial preservatives, and that this was evidenced by the fact that the entire product of at least fifty, and probably more, leading American food preservers, is entirely free from these substances. Speaking specifically of benzoate of soda the lecturer contended that so long as a doubt exists as to its harmlessness or harmfulness, the people rather than the manufacturers should be given the benefit of that doubt. After calling attention to the use of this chemical as a preservative for cannery waste, which is worked up into ketchups and soups, and for other similar purposes, the lecturer stated that he had no hesitation in saying "that the principal use of benzoate of soda and like substances in modern food manufacture, is either to permit the use of a lower grade of material, or carelessness in process."

In concluding his address Mr. Dow said that sterilization is the chief reliance of the modern food preserver, and that in the case of fruits and vegetables in which the color or taste would be affected by a comparatively high temperature intermittent sterilization at low temperature is employed.

F. Y.



APRIL PHARMACEUTICAL MEETING.

The stated pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday, April 19, at 3 o'clock, Henry C. Blair presiding.

Mr. Edgar F. Heffner, of Lock Haven, Pa., secretary of the Pennsylvania State Pharmaceutical Association, presented a paper calling attention to the work of that Association and setting forth some of its present aims, particularly along legislative lines, which will be published in a later number of this JOURNAL. In introducing Mr. Heffner the chairman spoke of the efficiency of his work as secretary of the Association and remarked upon the promptness with which the annual volume of Proceedings had appeared.

The paper elicited a prolonged discussion which centred mainly on the proposed State Antinarcotic Law, a subject made doubly interesting by reason of the crusade being waged at present in Philadelphia by the State Pharmaceutical Examining Board for the eradication of the cocaine evil. Among those participating in the discussion were Wm. E. Lee, chairman of the Pa. Ph. A. Membership Committee, L. L. Walton, chairman of the Committee appointed by the Association to draft a model Antinarcotic Law, Henry Kraemer, Theodore Campbell, a member of the Pennsylvania State Legislature, Otto W. Osterlund, C. B. Lowe, C. A. Weidemann, E. M. Boring, and Messrs. Heffner and Blair.

Mr. Walton stated that his committee had not as yet drafted the proposed law, as they had been waiting for Congress to frame a national law with the object of making the Pennsylvania State Law conform to it. He said that they had asked the opinions of druggists in all parts of the State as to the character of such a law, and he then read extracts from the acts of the following states: Massachusetts, Virginia, New Jersey, Michigan, Florida, Idaho, Alabama, Wyoming and Wisconsin. According to *The Apothecary* (April, 1910, p. 14) the provisions of the new Massachusetts Narcotics Law, as finally enacted, are as follows:

Under this law it is now unlawful for any person to sell, furnish, give away or deliver any opium, morphine, heroin, codeine, or preparations thereof, or any salt or compound of the foregoing substances, except upon the written prescription or order of a lawfully authorized practitioner of medicine, dentistry or veterinary medicine, which prescription must bear the name of the person giving it; provided, that the provisions of this section shall not apply to sales made by any manufacturer, wholesale or retail druggist, to other

manufacturer, wholesale or retail druggists; nor to sales made to hospitals, colleges, scientific or public institutions, or to physicians, dentists or veterinary surgeons; nor to the sale of cough remedies and other domestic and proprietary preparations; provided that such preparations are sold in good faith as medicines, and not for the purpose of evading the provisions of this act, if such preparations do not contain more than two and one-half grains of opium, or one-third of a grain of morphine, or one-fourth of a grain of heroin, or one grain of codeine or their salts in one fluidounce; or if a solid preparation, in one avoirdupois ounce, excepting liniments and ointments which are prepared for external use only; nor to preparations containing opium or any of its salts, which are sold in good faith, for diarrhœa, cholera or neuralgia; nor to powder of ipecac and opium, commonly known as Dover's powders; nor to compound medicinal tablets, pills or powders containing not over one-twentieth of a grain of morphine, or one-twelfth of a grain of heroin or one-fourth of a grain of codeine, or any of their salts to each pill, powder or tablet; provided, that such preparations are sold in good faith as medicines and not for the purpose of evading the provisions of the act.

Mr. Walton further remarked that personally he was in favor of reasonable legislation, that he believed that the legitimate uses of opium and morphine should be considered and that in enacting an antinarcotic law no necessary impediments should be placed in the way of such use. He said that the handling of habitues presented a difficult problem, as to prohibit entirely the use of the drugs to which they were addicted, would no doubt end in collapse and possibly death in some instances. Mr. Walton added that he had written a prominent New York firm asking for the record of their sales of cocaine, and that the firm's reply was that they were not required by law to keep a record of sales of this drug outside the State of New York.

Professor Kraemer said that the Pennsylvania cocaine law appeared to be very effective and that it ought to be a comparatively easy matter to introduce a clause providing for the similar regulation of the sale of morphine and its derivatives. He pointed out that in framing legislation of this kind the work of local, state and national organizations should be co-ordinated, and expressed the opinion that an interstate law bearing on the sale of poisonous drugs will probably be framed ere long, as this is a matter in which some of the Government departments have much interest.

Regarding the dose of morphine used by habitues, Mr. Lee stated that an instance had come to his notice where 15 grains were used daily, and Mr. Blair stated that he had understood that the taking of 1 drachm daily was not unusual.

Mr. Campbell stated that he had never sold morphine to habitues, and that he had had no opportunity of ascertaining the amount of the drug used by them. He was of the opinion that there would be no difficulty in getting the Pennsylvania State Legislature to pass a law regulating the sale of morphine and codeine so long as it did not apply to household remedies containing them, for immediately the question would arise as to what the people in the outlying districts would do. Mr. Campbell felt that there were a good many loopholes and "good faiths" in the Massachusetts law, and thought that the proposed Pennsylvania draft should not have these.

Mr. Osterlund coincided with this latter view, and stated that having been acting as a juror recently, he found that lawyers have no trouble in getting around the "good faith" clauses. He stated that the laws in the western states appeared to have fewer of these.

Dr. Lowe spoke of one drug store where a profit of \$60 a day was made from the sale of cocaine. He discussed the treatment of habitues, and said that one could hardly imagine the tortures of habitues when deprived of the drug, and referred to one case where 13 grains were taken at a dose and another instance where the daily dose was  $\frac{1}{3}$  ounce.

Dr. Weidemann said that he favored one feature of the proposed antinarcotic law, which Mr. Walton mentioned, namely, the drafting of the law in such a manner as to take into consideration the question of habitues. In this connection he mentioned the case of a dressmaker who he said had taken 2 fluidounces of the tincture of opium every day for the past forty years, and he felt that it would be wrong to deprive such an one of the drug. On the other hand, he said that something should be done, and that it was better to take measures to prevent the formation of the habit than to try to cure habitues.

Mr. Walton remarked at this point, that while the Massachusetts law has too many loopholes, it is still an example of what can be done. He said that there is only one way to accomplish the end sought, and that is by restricting the sale of morphine and this class of drugs to prescriptions, and then asked if any of those present thought that this could be accomplished.

Mr. Heffner spoke of the case of a young girl who used a pint of laudanum a week, and stated that she had recently been taken to a hospital for treatment by the administration of gradually decreasing doses of the drug, and that the result would be reported.

Mr. Blair, referring to Mr. Walton's question as to whether Pennsylvania ought to have a stringent morphine law, said that in his store, which is a very old one and owned successively by his grandfather, his father and himself, no morphine had been sold over the counter for three generations, and that at the present time he does not sell laudanum over the counter. He gave it as his opinion that morphine should not be sold to habitues, and said that he would favor a stringent law provided that it could be enforced. He said that there were eight habitues of the drug in his block, one of them being a total wreck, but that none of them ever came into his store for the drug.

Following the discussion of Mr. Heffner's paper Professor Kraemer called attention to the circular letter which had been sent out by Dr. Reid Hunt, chairman of the Committee on U. S. Pharmacopœia of the American Medical Association, asking for opinions regarding the function and scope of the Pharmacopœia and as to the general principles which should govern admissions and deletions. Those taking part in the discussion of the questions formulated in the circular were Dr. Horatio C. Wood, Jr., Dr. George D. Rosengarten, F. M. Apple, Professor Kraemer and Mr. Blair.

Methods for increasing the attendance at the annual meetings of the Pennsylvania Pharmaceutical Association were discussed by Messrs. Lee, Blair, Campbell, Boring, Lowe, Osterlund and Weidemann.

At the close of the discussion, Professor Kraemer called attention to a growing plant of *Sarracenia vario* which had been sent from Tampa, Fla., by Hamilton Russell, P.D., and to one of a fossil fern obtained from the coal mines of Shenandoah, Pa., and presented by Roy Hughes, a student of the College.

A vote of thanks was tendered the speakers of the afternoon and the donors of the specimens.

FLORENCE YAPLE,  
Secretary pro tem.



## MEDICAL EDUCATION IN THE UNITED STATES AND CANADA.

A report to the Carnegie Foundation for the advancement of teaching, by Abraham Flexner, with an introduction by Henry S. Pritchett, President of the Foundation, New York, 1910.

This volume of 346 pages is to be had, practically for the asking, and should be read, studied, and inwardly digested by every physician, every pharmacist, and every educated layman in these United States.

Part I consists of 180 pages divided into 14 chapters, and presents a survey of the history of medical education in this country, and a comprehensive discussion of the various problems that are involved in the present day effort to advance the requirements as well as the scope of medical education.

Part II contains a detailed report of the observations made in the course of a systematic inspection of the medical schools of the United States and Canada. This portion of the report is alphabetically arranged by states and provinces and includes, among other information, statistics relating to the population of the several states, the number of physicians and the ratio of physicians to inhabitants.

The report also discusses the more important local features and records in detail, the requirements, resources and facilities of the several schools.

An appendix contains a table showing the number of professors and other instructors in the faculty, the enrolment, fee income, and the budget of the several schools by states.

Finally, a rather complete index of 8 double column pages facilitates reference to any one particular feature or institution that is discussed.

No book published in recent years is destined to have a more far-reaching influence on the development of the educational institutions of our country, and therefore on the progress and wellbeing of the people themselves, as this volume which depicts in terse but always readable language the development or lack of development of the widely varying institutions more or less loosely classed as medical schools.

The President of the Foundation, in the introduction, points out that "one of the problems of the future is to educate the public itself to appreciate the fact that very seldom, under existing conditions, does a patient receive the best aid which it is possible to give

him in the present state of medicine, and that this is due mainly to the fact that a vast army of men is admitted to the practice of medicine who are untrained in sciences fundamental to the profession and quite without a sufficient experience with disease."

As an illustration of the inadequate nature of medical training, at the present time, it is pointed out that nearly one-half of the 150 medical schools in this country have an annual income of less than 10,000 dollars, while by far the greater number of schools attempt to limit their expenses to the fees received from students.

The existence of so many weak or inefficient medical schools would indicate a lack of professional patriotism on the part of those who were instrumental in their founding while the fact that at the present time the number of weak schools is actually being reduced, despite the monetary loss that is necessarily involved, is perhaps the most significant indication of progress in matters medical.

It should be noted that, indirectly, this book is the most severe arraignment of pharmacy, its ideals and its achievements that one would care to see. Looking ahead there is no mistaking the evidence that it is an indication of what we as pharmacists must measure up to, if we wish to continue to take an active part in developing the sciences of medicine and it most assuredly constitutes a warning that should not be ignored.

Some day, and that perhaps not in the far off future, the spirit, ideals and facilities of our pharmaceutical schools will be investigated and commented upon much in the same way as are the resources and possibilities of the medical schools in this volume.

So long as pharmacy essays to be an integral part of medicine it must live up to and comply with the requirements that are being made of those engaged in the practice of medicine itself, and pharmaceutical schools dare not lag far behind the requirements that are being made of medical colleges.

To the American Medical Association the active members of which have done and are now doing such yeoman service in calling attention to the overproduction of uneducated and ill-trained medical practitioners, this volume is a tribute that no amount of disparagement by otherwise interested individuals can counteract.

As noted above, however, every pharmacist who is interested in the progress of the sciences of medicine or in the public welfare should read and ponder over this report for himself.

The book may be obtained by enclosing 17 cents for postage with a request to: The Carnegie Foundation for the Advancement of Teaching, 576 Fifth Avenue, New York.

M. I. WILBERT.





TUBEROUS ROOT OF *Ipomoea Horsfallia*, HOOKER

About one-half actual length



# THE AMERICAN JOURNAL OF PHARMACY

AUGUST, 1910

## CHEMICAL EXAMINATION OF THE TUBEROUS ROOT OF *IPOMŒA HORSFALLIÆ*, *HOOKE*R.

BY FREDERICK B. POWER AND HAROLD ROGERSON.

A Contribution from the Wellcome Chemical Research Laboratories, London.

In the Spring of 1909 one of us was kindly presented by Mr. E. M. Holmes, F.L.S., Curator of the Museum of the Pharmaceutical Society of Great Britain, with a large tuberous root which had been received from the West Indies, and was evidently the product of a species of *Ipomœa*. It had been sent to Mr. Holmes by Messrs. Westmacott & Son, of Manchester, England, who had likewise favored him with the following information concerning it. "It grows wild, and is not cultivated for any purpose. This specimen was gathered in the woods of Maypen, Clarendon District, Jamaica, by our client, Col. Barlow, of Bury, who states that it is used for starch making, although it produces a yellow product, and that it is also used for food in some instances."

The root in question was a very large one, and, as it could not conveniently be preserved in its entire, fresh state, it was thought that it might be utilized for a chemical examination, so far at least as the amount of material would permit. Some additional interest was imparted to the subject by the fact that the present authors had recently made a complete chemical study of the stems of *Ipomœa purpurea*, Roth,<sup>1</sup> and also of the official jalap,<sup>2</sup> from *Ipomœa Purga*, Hayne (*Exogonium Purga*, Benth).

In order to ascertain the botanical source of the root referred

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<sup>1</sup> This JOURNAL, 1908, 80, pp. 251-286.

<sup>2</sup> Journ. Amer. Chem. Soc., 1910, 32, pp. 80-113.

to, Mr. Holmes had obtained from Jamaica, through the kindness of Col. Barlow, specimens of the flowering plant which produced it, and these were found to agree completely with the *Ipomæa Horsfalliæ*, as described by Sir W. J. Hooker, who established the species (compare *Botanical Magazine*, N. S., Vol. viii, tab. 3315. *Ind. or.*). Although the *Ipomæa Horsfalliæ* is described as an East Indian species, there would appear to be no doubt respecting the botanical identity of the plant received from Jamaica, where it must have been introduced. The remarks of Sir W. J. Hooker (*loc. cit.*) concerning the plant to which he had given the above-mentioned name may be deemed of sufficient interest to record in this connection.

In so extensive a genus as the present, and where many of the species are necessarily very imperfectly described, it behooves us to constitute new ones with great caution; and it is not until a careful comparison of the present individual, unquestionably one of the most beautiful, with all the descriptions to which I have had access, and with a most extensive collection of the genus in my herbarium, that I have considered it to be new, and have given it the name of the lady to whose kindness I am indebted for the drawing. The seeds were received by Charles Horsfall, Esq., either from Africa or from the East Indies, and raised by his very skilful gardener, Mr. Henry Evans, at Everton, where the plants produced their lovely blossoms in great profusion during the months of December and January (1833-4), a season when so gay a visitor is particularly welcome to the stove. Mr. Evans informs me that he has it under the name of *I. pentaphylla*; but the species so called by Jaquin has hairy leaves, and is in other respects quite a different plant, while the *I. pentaphylla* of Cavanilles (*I. Cavanillesii*, Roemer et Schultes) is still more at variance with our species. *I. Horsfalliæ*, in its inflorescence and blossoms, bears the closest affinity with *I. paniculata*, Br. (*Convolvulus*, L.), but their foliage is so different that the two plants can never be confounded: the former having compound and quinate leaves, while those of the latter are simply lobed.

#### EXPERIMENTAL.

The tuberous root of *Ipomæa Horsfalliæ*, Hooker, which formed the subject of the brief investigation here described, is represented in the plate accompanying this paper. It was light brown in color, with darker colored spots, and showed in places an exudation of black resin. The length of the root was 0.38 metre, its circumference at the largest part 0.37 metre, and it weighed 2395 grammes. The presence of an abundance of starch was evident when a section of the root, moistened with iodine, was observed under the microscope.

The root was sliced, and then dried in a water-oven, when it weighed 408 grammes, the loss of weight in drying having thus been 1987 grammes, or nearly 83 per cent. The dried material was ground to a fine powder, when it amounted to 385 grammes. It was then brought into a large Soxhlet apparatus, and thoroughly extracted with hot alcohol, the greater portion of the alcohol being subsequently removed, and the resulting extract distilled in a current of steam. The distillate was found to contain only traces of formic and butyric acids.

After the above-described treatment, the contents of the distillation flask consisted of a dark red, aqueous liquid, together with a small amount of resinous material. The liquid was filtered, and the resin repeatedly washed with hot water, after which the resin was dissolved in a little alcohol, the solution evaporated to dryness, and the residue dried at 100° C. The amount of resin obtained was 9.6 grammes, thus corresponding to 2.5 per cent. of the weight of dried, or 0.4 per cent. of the weight of the entire fresh root.

The resin formed a dark brown, spongy mass, which became somewhat sticky on exposure to the air. It was found to be almost completely soluble in ether.

#### *Optical Rotation of the Crude Resin.*

The optical rotatory power of the convolvulaceous resins has been considered to afford some indication of their identity or purity.<sup>1</sup> As this factor has previously been determined for several such resins, including those of *Ipomæa purpurea*, Roth, and jalap by the present authors,<sup>2</sup> it was deemed of interest to make this determination with the resin under examination. For this purpose 1.0 gramme of the crude resin was dissolved in absolute alcohol, and the solution treated with successive small quantities of animal charcoal until it was nearly deprived of color. The rotation of this liquid in a 2 dm. tube was  $-0^{\circ}54'$ , and the amount of substance contained in 10 c.c. of the liquid, after drying at 105–10° C., was 0.1584 gramme, whence  $[\alpha]_D -28.4^{\circ}$ . It may be noted that this degree of optical

<sup>1</sup> Compare Guigues, *Journ. de Pharm. et de Chim.*, [6], 22, 241, and *Chem. Centralblatt*, 1907, Bd. I, p. 309. Also *Bull. soc. chim.* [4], 3, 872, (1908).

<sup>2</sup> This JOURNAL, 1908, 80, p. 253, and *Journ. Amer. Chem. Soc.*, 1910, 32, p. 85.

activity is considerably lower than that of either of the above-mentioned resins, and appears to approximate most nearly to that of the resin from *Ipomæa orizabensis*, Ledanois, which has been recorded by Guigues (*loc. cit.*) as varying from  $-23.30'$  to  $-25^{\circ}$ .

*Extraction of the Resin with Various Solvents.*

A small portion of the resin (1.0 gramme) was reserved for a physiological test, and the remainder (7.6 grammes) dissolved in alcohol, the solution being brought onto prepared sawdust, and the mixture thoroughly dried. It was then successively extracted with light petroleum, ether, and alcohol, when the following amounts of extract, dried at  $100^{\circ}$  C., were obtained:

Petroleum (b. p. $40-60^{\circ}$ C.)	extracted 4.92 grammes, or 64.7 per cent.
Ether	extracted 1.90 grammes, or 25.0 per cent.
Alcohol	extracted 0.60 grammes, or 8.0 per cent.
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Total	7.42 grammes, or 97.7 per cent.

*Petroleum Extract.*—This was a soft, brown resin. It was heated in a reflux apparatus with an alcoholic solution of potassium hydroxide for several hours, after which the alcohol was removed, water added, and the alkaline mixture extracted with ether. The ethereal liquid was dried, and the solvent evaporated, when a small quantity of solid material was obtained. This yielded a little of a crystalline substance, which melted at  $132-133^{\circ}$  C., and gave the color reactions of the phytosterols.

The alkaline liquid which had been extracted with ether was acidified, and again extracted with this solvent, the ethereal liquid being dried and evaporated. A small amount of acid was thus obtained, which was distilled under diminished pressure, when it partially solidified. The oily portion was unsaturated, since it absorbed bromine in chloroform solution. The solid portion was recrystallized from dilute acetic acid, when it melted at  $56-58^{\circ}$  C. It was thus evident that the original product consisted of a mixture of acids, but the amount was too small to permit of their further separation.

*Ether Extract.*—This extract, like the preceding one, was a soft, brown resin. On redissolving it in ether a very small amount of a sparingly soluble substance separated, which was collected. This was found to give a color reaction similar to that yielded by



the phytosterols, and it probably consisted of one of the dihydric alcohols, such as ipuranol and ipurganol, which have previously been isolated by us from convolvulaceous resins (*loc. cit.*) and other sources. The exceedingly small amount of this substance rendered it impossible to identify it.

The ethereal liquid was subsequently shaken successively with solutions of sodium carbonate and sodium hydroxide, but only resinous material was thus removed, and on finally evaporating the ether only a trace of yellow resin remained.

*Alcohol Extract.*—This extract, which was very small in amount, resembled the two preceding ones, and even after prolonged drying it could not be reduced to a powder. Its alcoholic solution was treated with baryta, and allowed to stand in a warm place for twelve hours, after which the alcohol was removed, water added, and the barium precipitated by means of sulphuric acid. The filtered aqueous liquid did not reduce Fehling's solution until after heating with a drop of concentrated sulphuric acid, thus indicating that at least a portion of the alcoholic extract of the resin was glucosidic.

#### *Examination of the Aqueous Liquid.*

The aqueous liquid, as above indicated, represented that portion of the alcoholic extract of the root which was soluble in water, and from which the small amount of resinous material had been removed. It was first shaken with ether, and on adding to the ethereal liquid a little aqueous alkali the latter solution showed a blue fluorescence. This was probably due to the presence of traces of  $\beta$ -methylæsculetin,  $C_9H_5(CH_3)O_4$ , a substance which we have previously shown (*loc. cit.*) to be a constituent of jalap resin.

After extracting the aqueous liquid with ether, it was treated with a solution of basic lead acetate, which produced a light brown precipitate. This was collected, washed with water, and then suspended in water and decomposed by hydrogen sulphide. On filtering the mixture a liquid was obtained which gave a slight brown coloration with ferric chloride, but it yielded nothing definite. The filtrate from the lead subacetate precipitate was treated with hydrogen sulphide for the removal of the excess of lead, and again filtered. On concentrating this liquid a dark colored syrup was obtained, which contained a quantity of sugar, since it readily yielded *d*-phenylglucosazone, melting at 213–214° C.

In order to ascertain whether the resin obtained from the root of *Ipomæa Horsfalliæ*, Hooker, possesses any physiological activity, a test was kindly conducted for us by Dr. H. H. Dale, Director of the Wellcome Physiological Research Laboratories. One gramme of the resin was administered to a small dog, but no purgation was produced, nor could any other effect be observed.

It is evident from the results of the preceding investigation that the root of *Ipomæa Horsfalliæ*, Hooker, does not possess any constituent which would render it of medicinal value, for even the very small proportion of resin which it contains appears to be devoid of any marked physiological action.

In conclusion we desire to express our thanks to Mr. E. M. Holmes, F.L.S., for the great pains he has taken to secure the botanical identification of the material supplied to us.

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## THE BIOLOGICAL STANDARDIZATION OF DRUGS.\*

BY ROBERT A. HATCHER and J. G. BRODY.

Laboratory of Pharmacology, Cornell University Medical College.

This comprehensive title was chosen by one of us some months ago with the intention of presenting brief outlines of a number of methods of biological standardization which retail pharmacists would find available.

Since then we have been devoting most of the time at our disposal for the purpose to the study of one group of drugs and we shall therefore limit the scope of the paper to a single method, and a consideration of some of the drugs for which the method is adapted.

Crawford (AM. J. PHARM., vol. 80, 1908, p. 321) has given an excellent review of a number of the more important methods of biological assay. He says: "The group of digitalis, strophanthus, and squill is the most important one which we as physicians have to use, and it urgently demands standardizing." He quotes Naunyn as saying that he would not care to be a physician without digitalis. He also quotes Dixon as saying: "For my part I unhesitatingly

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\* Read in the Scientific Section of the American Pharmaceutical Association, at Richmond, Va., May 2-7, 1910.

express the belief that many hundreds of patients die annually from digitalis and allies not possessing the virtues required of them." To the foregoing we would add that we are equally convinced that the want of precise methods of dosage is responsible for many cases of poisoning with digitalis, and it is with this group of drugs that we have been engaged for the most part.

We are aware that many will raise the objection that the details of biologic assays are of little more than theoretical importance to the retail pharmacist because he is unable to conduct these operations. We believe that the progressive pharmacist must be prepared to make the simple biologic tests at least, if he is to pretend to keep pace with the progress of his profession, and it is our purpose to outline the technic of our method, which is so simple that it may be mastered by the retail pharmacist, and conducted with the apparatus which he has at hand.

H. C. Wood, Jr., has recently sought to convey the impression that it is hopeless to expect any degree of precision by means of the test on animals even when it is conducted by the trained pharmacologist. Wood says: "And first I shall speak of its limitations. We sometimes read of the physiological test being used as a control of the chemical assay. To attempt to corroborate the findings of the chemist by a test on the living animal is about as sensible as it would be for a navigator to regulate his chronometer by an Ingersoll watch; the relative accuracy of the chemical and physiological assay is about the same as that of the \$200 chronometer and the dollar watch."

To this statement we wish to enter certain exceptions.

METHOD.—The method of standardization which we have chosen for the digitalis group and some other drugs, consists in determining the minimal fatal dose per kg. of cat when the drug is injected slowly into the femoral vein, the standard chosen for the digitalis group being the cat unit.

The cat unit may be defined most accurately perhaps, as the amount of crystalline ouabain<sup>1</sup> which is fatal within about ninety minutes to a kilogramme of cat when the drug is injected slowly and almost continuously into the femoral vein. A cat unit is equal to almost precisely 0.1 mg. of crystalline ouabain, or one ten-millionth of the weight of the animal.

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<sup>1</sup> The older term ouabain is to be preferred to that of crystalline strophanthin which has lead to much confusion.

We would prefer this definition of the cat unit rather than that which would embrace any digitalis body required to produce a similar effect within the same period of time when used in this way. The reasons for this will be apparent from the discussion of the method.

When crystalline ouabain, amorphous strophanthin, or a preparation of strophanthus is to be tested, it is only necessary to inject the solution from a syringe or burette into the femoral vein until the animal begins to show toxic symptoms. The injection is then interrupted, or continued more slowly until the unmistakable signs of approaching death are seen. These signs are so typical that one is rarely mistaken concerning them. They consist in irregularity of the heart, difficult respiration, convulsions, and frequently a peculiar cry, after which recovery is extremely rare. If death does not occur in a few minutes the injection is continued with extreme caution.

Other members of the digitalis group may be tested in the same way, but the results will be somewhat too high as a rule, and in that case the necessary correction, usually amounting to about 20 per cent., may be made, or the assay may be made more accurately by a modification of the technic. Somewhat more uniform results are obtained if about 75 per cent. of the total amount of the digitalis body is injected in the first fifteen minutes and the remainder in the following hour. These results will still be too high, and we have therefore devised a modification of the method of estimating some of the other digitalis bodies which gives results which we believe to be nearly as accurate as those obtained with crystalline ouabain itself.

It might be better to explain the reason for this modification first, but for convenience the discussion will be given later.

Just as the analytical chemist may find it desirable to determine the alkalinity of a liquid by adding an excess of acid and titrating back with an alkali, so we have been able to obtain more accurate results in some cases when we inject a measured amount of the digitalis body (tincture or infusion of digitalis, or digitoxin) in the first period of about ten minutes, and after an interval of twenty minutes continue the injection, substituting a solution of crystalline ouabain for that of the digitalis body under examination until the death of the animal, or until the toxic symptoms appear. Naturally, we assured ourselves that ouabain was capable of replacing the other digitalis bodies before we adopted this method.



The difference between the amount of crystalline ouabain actually used to complete the assay and 0.1 mg. per kg. of animal (the amount which would have been required in the absence of the digitalis body), represents the activity of the digitalis used.

The following example will illustrate the mode of computing the activity of the digitalis body tested: A tincture representing 70 mgs. of digitalis per kg. of cat was injected into the femoral vein and after twenty minutes the injection of a solution of ouabain was begun. The animal died with the typical symptoms of digitalis poisoning when 0.0142 mg. of the crystalline ouabain per kg. had been injected. The difference between 0.0142 mg. and 0.1 mg. (which would have been required had the ouabain been used alone) is 0.0858 mg. or 85.8 per cent. of a cat unit, hence 70 mgs. of digitalis equals 85.8 per cent. of a cat unit, and 81.6 mgs. of the digitalis equals one cat unit. A duplicate experiment gave 81.8 mgs. of digitalis. That the results obtained by the modified technic are more accurate than those with the continuous injection of the digitalis alone is shown by a comparison of the results of the following experiments intended to fix the minimal lethal dose of digitalis by the vein with those given in Table III.

2/24/'10. Male cat, Wt. 3.65 kgs.

10.30 A.M. Injected 0.085 Gm. digitalis per kg. by vein at once.

10.45 A.M. Emesis. Cat lived over 7 hours, but died during the night.

4/9/'10. Female cat, Wt. 2.02 kgs.

11.40 A.M. Injected 0.080 Gm. per kg. by vein at once.

12.02 A.M. Emesis. (Repeated emesis.)

4/11/'10. Cat weighs 1.68 kgs., having lost 0.34 kg. in weight.

9.42 A.M. Injected 0.075 Gm. digitalis per kg. by vein at once.

9.58 A.M. Death occurred. (Cumulation.)

We have tested the following substances by intravenous injection into the cat: Crystalline ouabain, amorphous strophanthin, strophanthus seed, tincture of strophanthus, digitalis, tincture of digitalis, infusion of digitalis, digitoxin, digitalinum verum, digitalein, adonidin, digalen, amorphous digitoxin so-called, digipuratum, all belonging to the digitalis group, and German digitalin which does act

like digitalis when injected in this way, since it consists largely of digitonin which causes a sharp fall in the blood-pressure when injected into the vein. We examined digitonin and sparteine also, neither of them giving the digitalis action. Strychnine gave fairly uniform results, but the method requires careful control. Nicotine, physostigmine, and aconitine did not give concordant results in the experiments we made, and we have not been able to determine whether it is possible to modify the technic so as to make it available for those bodies or not.

TABLE I.

*Equivalents in mgs. per cat unit of various digitalis bodies.*

Ouabain, cryst. ....	0.10
Stroph. amorph. B. and S. ....	0.13 <sup>1</sup>
Stroph. amorph. Merck ....	0.17
Digitoxin, cryst. ....	0.30
Digitoxin, am. so-called ....	1.20
Digitalinum ver. Kil. ....	1.50
Stroph. hisp. ....	1.50
Digitalin ....	2.90
Adonidin ....	3.00
Stroph. Kombé ....	3.00
Digitalin, German ....	4.00
Digitalis, German ....	82.00
Digitalis, Eng. ....	92.00

The estimations in the table were made by the continuous injection of the various bodies mentioned except in the case of digitoxin and the digitalis leaf, and it is quite possible that corrections will have to be made for some of these when crystalline ouabain is used to complete the injection. Attention is called to the similarity of the results reported to those obtained by Worth Hale in comparing crystalline digitoxin with the amorphous so-called (*J. Am. Med. Assn.*, v. 54, p. 35), but we believe that the method reported here has the advantage of greater accuracy and ease with which it may be followed, and of great economy in time.

<sup>1</sup> This amorphous strophanthin of Boehringer and Sons sold in sterile tubes apparently is more active than other specimens of their amorphous strophanthin or that of Merck which we have examined at different times.

TABLE II.

	Mgs. dig. per cat unit.	Mgs. Dig. + ouabain.
A.	75.2	49 + 0.0351
A.	73.5	49 + 0.0333
B.	81.8	35 + 0.0572
C.	81.6	70 + 0.0142
D.	92.3	60 + 0.0350
D.	102.6	60 + 0.0414
E.	96.1	80 + 0.0168

The figures in the first column show the number of milligrammes of digitalis computed to equal 1 cat unit; those in the second and third columns indicate the digitalis and ouabain actually used.

TABLE III.

	Mgs. digitalis per cat unit.
A. Ger. (old) tr.	96.6
A.	91.0
A.	97.0
A.	122.0
B. Ger. (new) tr.	96.0
B. Ger. (new) tr.	98.7
C. Ger. (new) inf.	96.6
C. <sup>1</sup> Ger. (new) inf.	98.0
C. Ger. (new) inf.	103.0
D. <sup>2</sup> Eng. (new) tr.	113.7
D. <sup>2</sup> Eng. (new) tr.	113.7
D. Eng. (new) inf.	115.0
D. Eng. (new) inf.	122.0
D. Eng. (new) inf.	110.0
D. Eng. (new) inf.	106.0

The values in Table III were obtained by the injection of digitalis alone (c.f. Table II). A. represents a tincture obtained from leaf ground for percolation by Gilpin, Langdon & Co., in Oct., 1906. B. was from a specimen obtained from the same firm in April, 1910, and was said to have been obtained as recently as possible. D. was from an English leaf obtained at the same time as the German just

mentioned. It was said to be from a carefully collected and treated cultivated leaf.

C.<sup>1</sup> had had 100 mgs. of the same per rectum 3 hours previously.

D.<sup>2</sup> were labelled Mixt. A. and B., and the strength of these were unknown to the operator, Dr. Brody. In the first of these two experiments 2.73 c.c. per kg. were used, the cat weighed 1.65 kgs., hence 4.5 c.c. were injected; in the second 3.18 c.c. per kg. were used for a cat weighing 2.22 kg., a total of 7.05 c.c. The first solution represents 125 mg. in 3 c.c., and 3.5 c.c. of the second represents a like amount.

Four estimations of digitalinum verum were made. 1.50; 1.52; 1.56, and 1.80 mgs. respectively were found to be equal to 1 cat unit.

Digitalinum verum and digitoxin being insoluble in water, alcoholic solutions were employed.

Four estimations of digitalein were also made, the equivalents of a cat unit being 2.89; 2.90; 2.98, and 4.50 mgs. respectively. Digitalein being very soluble in water, is used conveniently in this way.

Two lactating animals were given large amounts of strophanthus in one case, and digitalis in the other. The first took 217 mgs. of digitalis per kg. of weight, which is more than twice the amount of this specimen usually required and the second took two and one-third times as much strophanthus as other cats of the same weight. These are the only two instances in which an animal required anything like so much of these two drugs. We are unable to state whether this is a coincidence or whether lactating animals are habitually tolerant toward the drugs of this group. We hope to be able to decide this point in the near future.

Three experiments were made with impure adonidin. The first animal received more than 6 mgs. of the drug per kg. of weight. We had little idea of the activity of the specimen and injected it much more rapidly than in the second and third experiments, hence the excess over that actually required was much greater. This experiment should be disregarded in the calculations. The second and third animals received 2.86 and 3.12 mgs. per kg. respectively.

The results obtained with German digitalin require an explanation. German digitalin is wholly unsuited for estimation by intravenous injection, its true digitalis action being much less than that indicated by the figures in the table, death being due mainly to the



digitonin of which it is chiefly composed. German digitalin probably has no place in digitalis therapy.

When the official preparations of digitalis, such as the tincture, are diluted with water a precipitate occurs, indicated by a faint opalescence, and in our earlier experiments we were unable to get uniform results when these diluted liquids were injected over a period of an hour or more. The injection of a large amount of alcohol is not permissible, and the use of concentrated preparations precludes the same degree of accuracy that is possible with the more dilute liquids. These objections are overcome, in part, by the combined method, in which ouabain is used to complete the estimation.

We have never seen any embarrassment of the respiration beyond some increase in the rate until the heart stopped. The immediate signs of asphyxia with excessive efforts at respiration showed that the respiratory centre was still intact. Furthermore, those drugs which kill by paralysis of the respiratory centre, usually give very variable results when used in this way. Strychnine is an exception, but there are many factors involved in the rapid action of strychnine, and it is quite possible that the sudden death following the intravenous injection is not due to its direct effects on the respiratory centre alone. The fact that the heart stops after all of the digitalis bodies before the respiration is seriously impaired is the strongest answer we can make to the contention of Edmunds and Hale (Hygienic Laboratory, Bulletin, No. 48, 1908), that methods which employ as a standard the minimum lethal dose for the higher animals are not applicable to the physiological assay of the digitalis series.

It is hardly necessary to state that it is a matter of vital importance that a standard shall be found for all the digitalis bodies in which the relative activity of the different members on the human heart may be expressed.

Hale found between 7 and 8 mgs. of digitoxin per kg. of frog, and 600 mgs. of digipuratum per kg. (*J. Am. Med. Assn.*, v. 54, p. 129) necessary to cause systolic standstill in an hour. This is sixteen times the amount of digitoxin, and eight times the amount of digipuratum, required per kilo for the cat's heart in our experiments. On the other hand, we have found less than twice as much strophanthus is required per kilo of frog as for the cat.

The following figures expressed in milligrammes per kg. of frog were obtained by Famulener and Lyons (*Proc. Am. Ph. Assn.*,

1902, p. 415). Digitalis leaf, 675; digitoxin, 8.7; strophanthus (5 per cent. tincture), 5.625; strophanthin, 0.5 (c.f. Table I); adonidin, 4. They state in their conclusions: Determinations of the relative strengths of different samples of the same drug may be made with precision sufficient for practical purposes by physiological experiments on animals, but, as might be expected, the relative medicinal strength of different drugs cannot be correctly inferred from the observation of a single symptom produced in an animal like the frog. They found differences of less than ten per cent. in duplicate experiments.

A further disadvantage in the use of the frog is due to the differences in the rate of absorption of the different digitalis bodies. Even such closely related bodies as amorphous and crystalline strophanthin differing markedly in this respect. Famulener and Lyons have also called attention to this objection.

We have attempted to compare the results which those authors obtained when working with the frog with those obtained by ourselves with the cat, but the differences are evidently due to differences in the animals and not to the limits of error.

Focke (Pharm. Zeitung, vol. 54, No. 68) says that after further consideration of the subject he believes that it is not feasible to accustom physicians to thinking and calculating the strength of digitalis preparations in frog units.

There are many reasons for believing that the action of the digitalis bodies on the cat's heart is a better index than that on the frog's of their effect on the human heart. Man absorbs strophanthin much as the cat and dog do, and the effects are much the same. Koppe's experiment in which 2 mgs. of digitoxin taken in dilute alcohol caused serious symptoms, shows the possibility of rapid absorption and unusual action; on the other hand, we know of instances in which 2 mgs. of crystalline ouabain have been administered intravenously without causing ill effects, though that is 25 per cent. of the theoretically fatal dose.

The cat is the least resistant to strophanthin and ouabain of all the animals which we have examined, but the rat and mouse alone, so far as our experience goes, are very resistant. There are marked differences in the subcutaneous and intravenous doses for the rabbit and some other animals, but not for the cat and the dog.

The various digitalis bodies are the subject of clinical investigation at the present time in certain of the hospitals in New York,

with the object of comparing their quantitative therapeutic action in connection with the results on the cat's heart, as shown by the experiments which we are conducting.

Naturally, minimal doses are being employed, but the comparative activity of crystalline ouabain and strophanthin even in the doses which have been recommended, seem to explain why positively brilliant results have followed occasionally the intravenous use of these substances.

We believe that the cat unit offers an easy means of computing the therapeutic dose of the various digitalis bodies when these are to be administered intramuscularly or by vein, but the rate of absorption from the alimentary canal must be determined before the oral use of these can furnish us reliable results.

That cumulation does occur with certain of these substances must be admitted, or, what amounts to nearly the same thing, the drug is not excreted or destroyed so readily in some cases as in others.

Strophanthin and ouabain may be repeated more frequently than digitalis, our incomplete investigations leading us to believe that the action of digitalis is far more persistent than is generally supposed.

We believe the outlook is more encouraging now than it has been at any time in the past for putting the therapeutics of digitalis upon a rational basis, but it must be admitted that we have no means at present of securing any degree of uniformity of action after the oral administration of these bodies, though it is not hopeless to look for one which will be absorbed readily from the alimentary canal, and we are endeavoring to find such a member of the group.

#### DISCUSSION.

*The Choice of the Animal.*—There are several reasons which influenced us to use the cat. These are in the order of their importance: Accuracy afforded, facility with which they may be obtained, ease with which they may be handled (contrary to common opinion), cheapness, and the fact that their use does not affect the sensibilities of the sentimental portion of the community to the same extent that the employment of the dog does.

*The Use of Ouabain to Complete the Reaction after Digitalis.*—It is commonly stated that digitalis acts slowly, thus Sollmann, Text-book of Pharmacology, 2nd ed., p. 488, says: "The action of the digitalis group is peculiar, in that it cannot be secured at once, unless

toxic doses are given intravenously. If this is done, the animal goes through all the stages; but even in this case, several hours are required until death occurs, no matter how much of the drug is given."

The latter part of this statement does not apply to the cat, nor does it apply to strophanthin so far as I am aware, nevertheless, it is true that moderate<sup>1</sup> doses of digitalis act much more slowly on the cat's heart than crystalline ouabain does, hence the interval that occurs between the injection of the minimal fatal dose and the death of the animal is longer with digitalis than it is with ouabain, and a greater excess of the digitalis will be injected during that interval. If approximately fifty per cent. of the fatal dose of digitalis is injected into the vein and twenty minutes are allowed to elapse and the injection is then continued using one part of crystalline ouabain in one hundred thousand parts of physiological salt solution, the end reaction is almost as sharp as with ouabain alone, the interval appearing to suffice for the digitalis to exert almost its full action on the heart.

The extraordinary uniformity<sup>2</sup> of the action obtainable with ouabain and other digitalis bodies on the cat's heart calls for some comment. We have been inclined to think that this might be explained by the absence of racial peculiarities, due to the nocturnal habits of the cat whereby cross breeding is almost universal. We are endeavoring to explain this uniformity, and while we believe there is a deeper significance than the one just suggested, we are not prepared to go deeply into a discussion of this phase of the question at present.

The fact that crystalline ouabain is capable of replacing amorphous strophanthin, as well as the digitalis bodies found in the leaf,

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<sup>1</sup> Massive doses of digitalis may cause death in 60 seconds, or about half the time required by the largest doses of crystalline ouabain. We believe that this extraordinary rapidity of action of digitalis is attributable largely to digitalein, which also acts rapidly.

<sup>2</sup> Since writing the preceding statement, which was based on a very large number of experiments covering a period of several years, we have found a number of cats which tolerated doses up to nearly fifty per cent. more than that stated. We are unable as yet to explain this. As previously stated, the only ones which succumb to doses below the standard are the excessively fat. The later observations do not prevent the use of this method of standardization, but a somewhat larger number of observations are necessary than would be otherwise.



so far as the direct action on the heart is concerned, lends support to the suggestion made by Schmiedeberg many years ago that all the members of the digitalis group depend on a similar nucleus for their action.

The use of this method of biological assaying and its remarkable accuracy have lead us into the investigation of some problems which we wish to mention at this time, though they have no immediate connection with the subject of the paper. We are employing it to show the degree of absorption which occurs after the oral administration of the various members of this group. The results show that absorption is exceedingly irregular with all of them which we have tested. By this means we have also found that the tincture of digitalis represents the activity of the leaf fully, the marc left after the preparation of the tincture from a specimen of the German digitalis in one case, and from the English in another, being inert. The same may be said of the infusion, at least a one per cent. infusion showed the same activity as the tincture diluted to the same strength, and, as just stated, this fully represented the leaf. We have also found in one case that a carefully prepared tincture of strophanthus, made according to the Pharmacopœial process, represented only about two-thirds of the total activity of the seed, despite the fact that percolation had been continued for one week. The greater part of the strophanthin which is extracted is removed during the first part of the percolation, a part of the strophanthin, or some related body, being removed slowly by percolation. The total active principles of the seed may be removed completely, so far as we have been able to determine, by infusing the finely powdered seed for one hour on a boiling water bath.<sup>1</sup>

The foregoing suggests a number of ways in which the biologic test may be utilized by the retail pharmacist.

Several interesting points are raised by the results with strophanthus recorded in Table I. A specimen of *Strophanthus hispidus* was

<sup>1</sup> Since this paper was read at Richmond we have tested a tincture of strophanthus made by the Pharmacopœial process and found that it did not represent the seed fully, but the marc yielded no active principle to boiling water. Another tincture prepared from the same specimen of seed after removing the fixed oil did represent the seed fully, 1 c.c. being equal to more than 60 cat units. This suggests that the active principle may undergo some change even during percolation or infusion.

It will be remembered that there is no difficulty in exhausting digitalis either by percolation or infusing the powdered leaf.

examined and the tincture and the infusion gave concordant results indicating that 3.5 mgs equalled 1 cat unit. A specimen of the Kombé showed exactly half the activity of the hispidus, 7 mgs. being found to be equal to a cat unit, a tincture and an infusion being likewise examined. Subsequently an authentic specimen of each, obtained from Professor Rusby, was examined, the seed being finely powdered and exhausted by heating on a boiling water bath for an hour. The ratio of activity of the infusions was the same as that just mentioned, but both infusions were much stronger than we had anticipated they would be, and 1.5 mg. of the hispidus and 3 mgs. of the Kombé were found to be equal to a cat unit. The activity of this specimen of hispidus corresponds to about 12 per cent. of Merck's amorphous strophanthin—an activity that has been hitherto unsuspected, we believe.

*Conclusions.*—The cat affords a simple method of standardizing the drugs of the digitalis group. This method is available for the retail pharmacist who will devote as much care to the process as is required in the chemical assay of opium.

The cat affords a means of comparing the activity of the several digitalis bodies on the human heart. This is not possible on the frog by present methods.

With some of the digitalis bodies, notably digitoxin, the minimal lethal dose for the cat by the vein is determined more conveniently by injecting about one-half of the lethal dose into the vein, and after an interval of about twenty minutes, injecting crystalline ouabain (so-called crystalline strophanthin) until the animal dies.

Crystalline ouabain is capable of replacing any of the digitalis bodies which we have tested so far as the direct action on the heart is concerned, that is, one-half of the fatal dose of any of these digitalis bodies and one-half of the fatal dose of crystalline ouabain will cause death in a short time if they be injected into the femoral vein in the manner described.

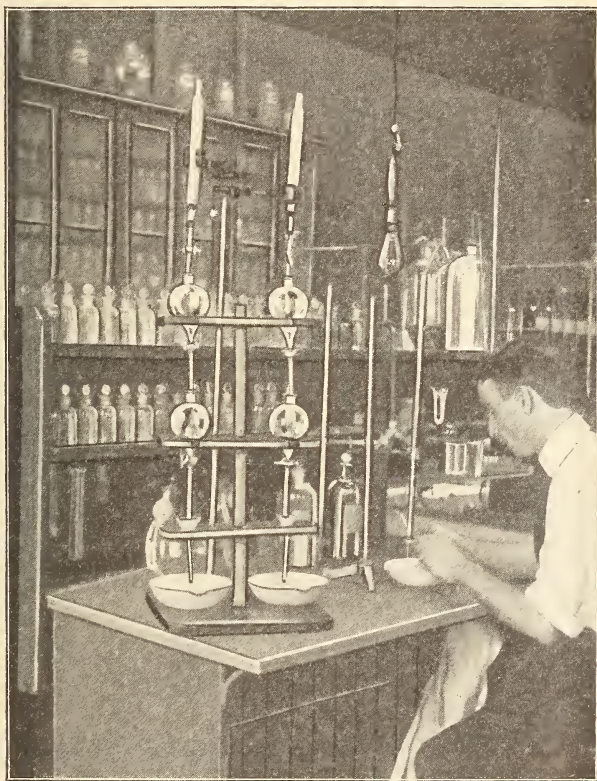
The absorption of digitalis and of strophanthus from the alimentary canal is extremely variable, that of strophanthus is far more variable than that of digitalis, for this reason the activity of these drugs cannot be fixed by means of the oral administration.

Cumulation occurs with digitalis to such a degree that no conclusions can be drawn regarding activity from the effects on animals which have been used previously for digitalis, unless many weeks have elapsed since the previous use.

## A RACK FOR HOLDING SEPARATORY FUNNELS.\*

By J. G. ROBERTS.

Recognizing the need of a simple and inexpensive separatory funnel holder, the apparatus shown in the accompanying illustration was designed. It is simple in construction and can be made by an



Rack for separatory funnels.

amateur carpenter. It consists of a base 15 in. square. In the centre is fastened an upright rod 22 in. high, and to this rod, which

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\* Presented before the Scientific Section of American Pharmaceutical Association at Richmond, Va.

passes through the middle of them, are fastened the arms which hold the funnels.

The arms are the same length as the base and in the case of the two upper ones are  $4\frac{1}{2}$  in. wide. The space between the supports is arranged so that the stem of one separator extends about one inch into the other. The openings to contain the separatory funnels are  $2\frac{1}{2}$  in. in diameter, and are wide enough to permit the bowl of the separator to extend about  $1\frac{1}{2}$  in. below the base of the support. A piece,  $\frac{1}{2}$  in. wide, is cut out in front of the support to enable the separator to be more readily replaced. The lowest support is the same length as the upper ones but is only 3 in. wide. It contains holes  $1\frac{1}{4}$  in. in diameter for small funnels, in which the last shake-out is filtered into beakers or dishes.

By means of this apparatus it is possible to start an alkaloidal assay in the upper separator, continue through the various shake-outs, and finally filter it directly into the beakers or dishes. Where a drug is to be extracted, Gordin percolators can be supported above the separator and the drug percolated directly into it.

ANALYTICAL DEPARTMENT, SMITH, KLINE & FRENCH CO.

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## PHARMACY AND THE U. S. PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.\*

Despite the fact that for upwards of a decade representatives of the Public Health and Marine-Hospital Service have regularly attended the meetings of the American Pharmaceutical Association there appears to exist, even among pharmacists, a lack of appreciation of the varied and far-reaching efforts to protect the health of the American people that are now being made by the several divisions of this service.

The Public Health and Marine-Hospital Service, as now organ-

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\*THE U. S. PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE. At the recent meeting of the American Pharmaceutical Association, in Richmond, M. I. Wilbert, one of the representatives of the Public Health and Marine-Hospital Service, in presenting the felicitations of the Surgeon General of that Service, offered for publication the appended description of the several activities of the present public health service, and called attention to the desirability of having pharmacists better informed regarding the work now being done, under the auspices of the service, for the protection of the public health.



ized, is a bureau of the U. S. Treasury Department, and had its origin, as the "Marine-Hospital Service," in 1798. This service was reorganized in 1870 and in 1902 its duties were materially augmented and its name changed to "Public Health and Marine-Hospital Service." The varied activities of the service are in a measure reflected by the titles of the administrative divisions which include: Marine hospitals and relief, domestic quarantine, foreign and insular quarantine, sanitary reports and statistics, and scientific research.

More detailed information regarding the activities of these several divisions is to be obtained from the service publications, which are classified under five heads: (1) Annual Reports, (2) Weekly Public Health Reports, (3) Public Health Pamphlets and Brochures, (4) Bulletins of the Yellow Fever Institute, and (5) Bulletins of the Hygienic Laboratory.

The importance of the work done in connection with quarantine service at domestic ports, is evidenced by the fact that during the fiscal year ending June 30, 1909, no less than 8266 vessels were inspected and 520 were disinfected as a precaution against yellow fever or plague. Foreign quarantine work includes investigations into the sanitary history of vessels destined for ports in the United States, the inspection of vessels, crews and passengers, and the fumigation or disinfection of ships when necessary.

The Division of Sanitary Reports and Statistics of the Public Health and Marine-Hospital Service collects information regarding the existence and prevalence of quarantinable diseases and the nature and effect of sanitary measures adopted by other countries.

Much of the scientific research work done in connection with the Public Health and Marine-Hospital Service is carried on in the Hygienic Laboratory. The original building of this laboratory, located at 25th and E Streets, N. W., Washington, D. C., was occupied in 1903, and the more recent extension was completed in 1909. It is a brick and sandstone structure, 230 feet long, two stories in height, with basement and attic, and contains 41 rooms.

The personnel of the Hygienic Laboratory, at the close of the last fiscal year, comprised a total of 55 persons: A director, an assistant director, 3 chiefs of divisions, 8 commissioned medical officers, 2 pharmacists, 11 technical assistants, an artist, and 28 attendants. To facilitate the pursuance of the scientific work, the laboratory is

divided into divisions more or less distinct and independent of each other. These divisions include

1. Division of Pathology and Bacteriology,
2. Division of Zoölogy,
3. Division of Pharmacology, and,
4. Division of Chemistry.

The work that has been done in connection with the several divisions of the Hygienic Laboratory has attracted widespread attention and is generally recognized as being of great scientific value.

As a practical illustration of the appreciation of this work by individual citizens, it is but necessary to call attention to the recent gift of \$1,000,000 by Mr. John D. Rockefeller for the purpose of eradicating hookworm disease from the Southern States. This gift is not alone a recognition of the scientific character of the work done in the Hygienic Laboratory, but is also a tribute to the ability and worth of the Chief of the Division of Zoölogy, who was the first to call attention to the now widely recognized prevalence of hookworm disease in the Southern States.

In addition to hookworm disease the Public Health and Marine-Hospital Service, largely in or under the auspices of the Hygienic Laboratory, has carried on extensive investigations on the causative factors and the possible prevention of tuberculosis, yellow fever, plague, leprosy, typhoid fever, pellagra, diphtheria, tetanus, rabies, and other infectious and contagious diseases.

The Hygienic Laboratory is by law entrusted with the supervision of the manufacture and sale of sera, vaccines, and similar products, and the Division of Bacteriology has evolved and perfected standards for antidiphtheritic serum and for antitetanic serum that have been accepted without question by the manufacturers of these products and have been favorably commented upon and endorsed by bacteriologists and scientists generally.

The Public Health and Marine-Hospital Service has been repeatedly accused of not giving to pharmacy the recognition that it rightfully deserves in public health work. That this accusation is unfounded and is, in fact, based on a misconception of what pharmacy itself is, or should be, is evidenced by the work now done in connection with the Division of Pharmacology of the Hygienic Laboratory.

Even at the present time this division of the Hygienic Laboratory

is exceeded in size and importance only by the Division of Bacteriology and Pathology, and the scientific work that has been done under the direction of its chief, Dr. Reid Hunt, is widely recognized as being of distinct scientific value. This work is particularly interesting in that it is of prophetic import; being representative of the future of pharmacy and indicative of the work that can be and very properly should be, done by the professional pharmacist if he is to continue as the accepted authority on information relating to drugs and medicines.

Much of the work that has been done up to the present time relates more or less directly to the materials included in the Pharmacopœia of the United States.

One of the earlier bulletins emanating from the Division of Pharmacology, included a discussion of the changes in the U.S.P. VIII, particularly the nature and properties of the new remedies that were included in that book.

More recent bulletins deal largely with compilations of comments on the Pharmacopœia of the United States and the National Formulary. These compilations are being prepared at the request of the Board of Trustees of the U.S.P. Convention, and, it is expected, will be of material assistance in the forthcoming revision of the U.S.P.

While much routine work is done in connection with the examination of chemicals and pharmaceutical supplies, the possibility of making original investigations is not lost sight of and the hours devoted to such investigations are by no means limited to the working hours prescribed by the Government regulations.

The publications emanating from the Division include communications on the study of the various suprarenal preparations, the standardization of preparations of the thyroid gland, the toxicity of acetanilid mixtures, the variability of and methods of standardizing preparations of digitalis, the solubility of pharmacopœial compounds, the melting points of chemical substances, and the application of the U.S.P. analytical methods to the purity rubric.

Even this meagre record should suffice to convince the most skeptical that in at least one of the Government Medical Services, Pharmacy, "*Pharmacia Vera*," has received proper recognition and that the work now being done in the Division of Pharmacology of the Public Health and Marine-Hospital Service is destined to open up for true pharmacy a field of activity that is as yet but imperfectly occupied.

## CORRESPONDENCE.

## THE PHARMACEUTICAL SYLLABUS—NATIONAL COMMITTEE.

DEAR SIR:

At a regular meeting of the National Committee held Thursday evening, May 5, 1910, at Richmond, Va., careful consideration was given the question of the completion and revision of the Pharmaceutical Syllabus.

The very favorable reception accorded this work, and the unanimity of opinion touching its importance, inspired the Committee to enter at once upon the task of harmonizing certain details and of adjusting other differences.

It was decided to ask the assistance of the boards of pharmacy and the faculties of the schools at the earliest practicable moment so as to have the study under way before the schools close for the summer vacation.

Therefore, without waiting for the completion of our reorganization, we are bringing this action to the attention of the secretaries of the faculty of each school of pharmacy and of each board of pharmacy.

Kindly secure criticisms and suggestions that may improve the syllabus from your point of view and report the same to the Secretary of the National Committee at the earliest practicable moment.

In the interests of pharmaceutical education.

Very respectfully yours,

WILLIS G. GREGORY, *Chairman,*

HENRY L. TAYLOR, *Secretary.*

Albany, N. Y., May 16, 1910.

## THE PHARMACEUTICAL SYLLABUS.

*Reorganization.*—The first edition was published February 18, 1910. The Committee of 21 thereupon entered on a discussion of the question of its completion and revision.

The New York State Board of Pharmacy, on the recommendation of the Committee, gracefully consented to its effacement from the leadership in this important movement by copyrighting the syllabus in the name of the National Committee. This action materially increases the responsibility of the National Committee by



placing on it the task of continuing the work and of issuing a revised edition.

To conserve the truest interests of pharmacy and thus to deserve the support of those national organizations most closely representing those interests, it was felt that the Committee should be reorganized so as to have a vital relation and be directly representative of the three great national bodies most deeply interested in the progress of pharmacy. On formal motion, it was

*Voted* to recommend that this responsibility be assumed by the American Pharmaceutical Association, through its Section on Education and Legislation, the American Conference of Pharmaceutical Faculties, and the National Association of Boards of Pharmacy.

These recommendations were made by the Chairman of the subcommittees at the Richmond meeting. As a result the American Pharmaceutical Association amended its By-Laws by increasing the number of Committees by one—"a committee on the Pharmaceutical Syllabus of seven members"—and provided for the appointing of members to the same by the President of the Association as follows: "One member shall be appointed for seven years and one for six, five, four, three, two and one years respectively; each vacancy occurring from the expiration of term shall be filled for a term of seven years; other vacancies shall be filled at the annual meetings of the Association for the unexpired terms. This committee shall report to the Association through the Section on Education and Legislation; shall be members of the National Committee on the Pharmaceutical Syllabus, and shall recommend to the Association its proportionate share of the current expenses."

The American Conference of Pharmaceutical Faculties provided a new By-Law to the same effect and provided for its proportionate share of the current expenses.

The National Association of Boards of Pharmacy amended its By-Laws in harmony with the same action of the other associations and provided for its proportion of the expenses.

Both the Conference of Faculties and the Boards' Association formally adopted the syllabus as a guide for future examinations, during the syllabus period.

Representatives were nominated and elected from the three associations pursuant to the amended By-Laws, and on Thursday evening, May 5, 1910, on formal call, the National Committee was

reorganized by the election of Willis G. Gregory, Chairman, and Henry L. Taylor, Secretary.

The Chairman was authorized to appoint the members of the various sub-committees and to make the work most efficient has given to each member a first and second choice as to assignment.

On formal motion, it was

*Voted* that for the purposes of special meetings called by the Chair, the quorum be seven.

*Voted* to ask the assistance of the boards of pharmacy and the faculties of the schools of pharmacy in the task of harmonizing certain details and of adjusting other differences with a view to the completion and revision of the syllabus in the near future.

*Voted* that each sub-division, as soon as appointed, take up the revision of its respective portion of the syllabus and report the same to the Secretary not later than October 1, 1910.

The Secretary was instructed to prepare suitable stationery and to preserve the certificate of copyright.

*The National Committee.*—The organizations they represent, the period of time for which appointed at the Richmond meeting, and their addresses that will secure quickest mail delivery.

AMERICAN PHARMACEUTICAL ASSOCIATION.—Willis G. Gregory, C. S. N. Hallberg, E. G. Eberle, Harry B. Mason, Charles Caspari, Jr., George M. Beringer, Henry L. Taylor.

BOARDS OF PHARMACY.—Ernest O. Engstrom, Samuel L. Hilton, Charles Gietner, Charles T. Heller, David F. Jones, Clarence O. Bigelow, Ernest Berger.

AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES.—James H. Beal, Henry H. Rusby, J. O. Schlotterbeck, Julius A. Koch, William C. Anderson, Clement B. Lowe, Henry V. Arny.

## BOOK REVIEWS.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. Fourth Edition. Volumes I and II. Edited by Henry Leffmann and W. A. Davis. Philadelphia: P. Blakiston's Son & Co., 1012 Walnut St. 1909, 1910.

Allen's commercial organic analysis is so well known to all those who are engaged in the assaying and examination of the various organic chemicals and products employed in the arts, manufactures, and in medicine, that the mere mention of a new edition is sure to be welcome news. Volume I deals with the alcohols, carbohydrates, yeast esters, aldehydes and vegetable acids, while in Volume II are given the fixed oils, fats and waxes, soap, glycerol and wool fat. The editors, who are also well known analysts, have been assisted by 13 contributors who are specialists in their respective fields. The text has been completely re-written and a very large amount of new matter has been added.

The present edition is an ideal laboratory manual in that "much descriptive matter now fully treated in text-books on chemistry and technology has been omitted" and with the aid of a large number of specialists, "each entrusted with the task of bringing a particular section up to date," there has been produced what is essentially a practical work on the properties and methods of analysis of organic substances.

There has been some re-arrangement in the distribution of some of the topics. The examination of malt has been transferred to the section on "Malt Liquors," where it belongs. The subject of Cellulose Nitrates has been transferred to the section on "Smokeless Explosives." The chemistry of explosives will be published in a separate volume to be published later.

The introduction, including methods of conducting organic analysis, has been written by Wm. A. Davis. The chapters on "Alcohols" and "Wines and Potable Spirits" were prepared by G. C. Jones. The article on "Malt and Malt Liquors" was prepared by Julian L. Baker. Emil Schliching wrote the monograph on "Yeast, Pure Culture Yeasts and Compressed Yeast." The chapters on "The Neutral Alcoholic Derivatives," "The Acid Derivatives of Alcohols" and "Soap" were prepared by Henry Leffmann.

E. Frankland Armstrong wrote the monographs on "Sugars" and "Starch and its Isomers." The portion on "Paper and Paper-Making Materials" is the work of R. W. Sindall. The monographs dealing with "Fixed Oils, Fats and Waxes" and the one on "Lard" were written by C. Ainsworth Mitchell. A chapter on "Special Characters and Methods" in the analysis of the fixed vegetable and animal fats is the work of Leonard Archbutt. The analysis of "Butter Fat" received the special attention of Cecil Revis and E. R. Bolton. C. A. Klein wrote the chapter dealing with "Linseed Oil." W. Robertson is the author of the chapter on "Higher Fatty Acids." "Glycerol" is considered in a special chapter by W. A. Davis. The chapter on "Cholesterols" is written by John A. Gardner. And Augustus H. Gill wrote the monograph on "Wool-Fat and Cloth Oils."

The work of each of the contributors has been well done. The editorial work and proof-reading by the editors is of exceptional quality. The printing and mechanical part of the work are excellent. It is not too much to say that these volumes of the new edition will be found indispensable to all analysts and students of organic substances.

H. K.

INTRODUCTION TO THE ANALYSIS OF DRUGS AND MEDICINES. An elementary handbook for the beginner. By Burt E. Nelson. 12 mo., ix+384 pages. Illustrated. New York, John Wiley & Sons, 1910. Cloth, \$3.00 net.

This work is, as stated by the author, of an elementary character and is intended as a handbook in determining the proximate analysis of drugs, medicinal chemicals and mixtures. It is expected to be useful to the student or analyst who has not specialized in drug chemistry. There are eleven chapters as follows: (1) Introduction; (2) Apparatus and Operations; (3) Ultimate Inorganic Analysis; (4) Ultimate Organic Analysis; (5) Determination of Molecular Weights, Common Radicles and Chemical Formulæ; (6) Principles and Methods of Drug Analysis; (7) Analysis of Medicines Generally; (8) The Principles of Microscopical Drug Analysis; (9) Systematic Microscopic Drug Analysis; (10) Assays of Chemicals, Crude Drugs and Pharmaceutical Preparations; (11) Pharmacological Methods. There are in addition 12 tables: (1) Systematic table of organic drug constituents and medicinal chemicals; (2) elementary organic analyses of medicinal chemicals, arranged in order



of their carbon content; (3) melting-points of commonly occurring medicinal chemicals and their derivatives; (4) boiling-point tables; (5) alcohol tables; (6) table of constants of fats and oils; (7) table of volatile oils; (8) glycerin tables; (9) resins, gum resins and balsams; (10) physiological action of some common drugs; (11) table of elements; (12) commonly used metric and English equivalents.

The work contains a large amount of valuable information which, however, is likely to be of more value to the trained analyst than the beginner.

H. K.

SQUIRE'S PHARMACOPŒIAS OF THE LONDON HOSPITALS. J. & A. Churchill, 7 Gt. Marlborough St., London, W. F'cap 8vo. Pages 496. Price \$5. Net.

This work contains a comparison of thirty of the pharmacopœias of the London hospitals. The idea of the book is to present its readers with a selection of formulæ, framed by heads of the medical profession attached to the various hospitals. The first edition of the London Hospitals' Pharmacopœia was published by the late Peter Squire in 1863, so that for nearly half a century this little book has been a recognized work of reference to the medical profession. It was an extension of the comparison of the three Pharmacopœias of London, Edinburgh, and Dublin, from which the first edition of Squire's Companion to the British Pharmacopœia was evolved. Another of the reasons for producing the first edition was the idea that a publication of a comparison in this form, might suggest to the different hospital authorities, when preparing the new edition of their respective pharmacopœias, whether it would not be advisable to modify many of their formulas so as to assimilate them to those of a like nature in the British Pharmacopœia and thus to simplify and reduce the number of compound drugs.

The seventh edition was published in 1900, and it is a noteworthy fact that in the subsequent 10 years no less than 26 of the London hospitals have produced new editions. So numerous and extensive have been the alterations in the formulæ that this eighth edition had to be practically rewritten. At the same time many new formulæ have been introduced. The work will be found valuable to members of the medical profession, as it represents select methods of prescribing very many drugs, and forms a practical compendium of

prescriptions framed by the leading authorities in the profession.

It will also be found extremely useful by dispensers, not only for the reasons given above, but because it will enable the dispenser often to understand and interpret the wishes of the prescriber, and afford him a ready reference to the recognized formulæ used in the various hospitals. It should prove a valuable counter adjunct.

Many of the sections are of more than ordinary interest, such as—*Collunaria*, *Gargarisma*, *Guttæ*, *Injectiones*, *Lotio*, *Mistura*, *Nebula*, *Pasta*, etc. The comparisons of peptonized foods and nutrient enemata are worthy of special attention, as they represent a very careful comparison and elaboration of the formulæ given in the various hospitals in which these subjects are dealt with.

A leaflet descriptive of the book, which reproduces typical specimen pages, and which briefly reviews its aims and objects, will be forwarded gratis to those applying for it, to—Squire & Sons, Chemists on the Establishment of His Majesty, The King, 413 Oxford Street, London, W.

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## OBITUARY.

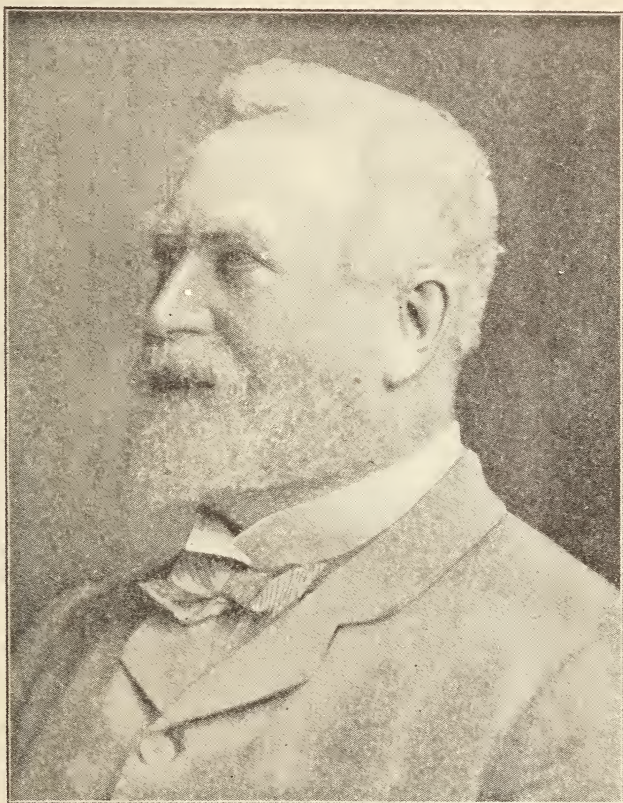
### MICHAEL CARTEIGHE.\*

It is with profound regret that we have to record the death of Michael Carteighe, which occurred at an early hour on the morning of May 30, 1910. Although those who knew him intimately were not wholly unprepared for the intelligence which it is our painful duty to communicate, the news will come as a shock to that large circle of acquaintances who in later years had known him only as a member of the Council of the Pharmaceutical Society. That circle embraced the whole of the pharmaceutical body at home, as well as

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\* Those of us who attended the Chicago meeting of the American Pharmaceutical Association, in 1893, well remember the striking personality of Michael Carteighe, then president of the Pharmaceutical Society of Great Britain and the bearer from that society of the Hanbury Medal to Prof. John M. Maisch, to whom it was awarded that year. The accompanying presentation address is published in the *Proceedings* of 1893, pp. 29-31. The writer also well recalls the presence of both Mr. Carteighe and Mr. Martindale on account of their participation in the discussions of the A. Ph. A. and those of the International Pharmaceutical Congress. Mr. Carteighe was an honorary member of the Philadelphia College of Pharmacy, having been elected in 1889.—EDITOR.

a large number of pharmacists in the Colonies and foreign countries, and men of science of all nationalities. Michael Carteighe was a scion of a County Cork family, though born in Lancashire in 1841.



MICHAEL CARTEIGHE.

He came to London at an early age, and received his preliminary scholastic training at a Clapham school. Later he served his apprenticeship to pharmacy with Mr. Radermacher, of New Cavendish Street, London, after which he became connected with University



College, Gower Street, first as a student and later as a Demonstrator in Chemistry, working under Professor Williamson. There he took part in many important chemical and physical researches, one of the most notable being an investigation of the electrical conductivity of alloys, wherein he was associated with Drs. Matthiessen and Holzmänn; the results of this work were embodied in a paper which was read before the Royal Society, and served as the basis of much subsequent work on the same subject. It seemed at this period as though the erstwhile pharmaceutical apprentice would be attracted permanently to a scientific career, but Fate intervened, and it was considered desirable that he should become fully qualified as a pharmacist, and join his elder brother in the conduct of the business with which the name of Carteighe has ever since been associated. Accordingly, the year 1862 found Michael Carteighe duly entered as a student at the Pharmaceutical Society's School of Pharmacy. He passed the Minor Examination on April 15, 1863, and three months later he passed the Major Examination. His success at the School gave promise of a successful and useful career—a promise which has been amply fulfilled. To say that he won the medal for chemistry and pharmacy, the medal for botany and materia medica, and the Pereira medal, would be to give but an inadequate idea of his scholastic achievements. A proper estimate of his work was formed by Redwood, who, as Professor of Chemistry and Pharmacy, in reporting the result of the competition in these subjects, stated that he took 800 marks as representing the highest value of the answers, and that one student had obtained 765 and another 710. The former was Michael Carteighe; the latter Charles Umney. Professor Bentley was equally complimentary. He said that of Michael Carteighe he could truly say he was an ornament to his teachers and to the school in which he was educated, and he felt sure that he would distinguish himself in his future career. The value of his answers at the written examination was at least equal to that he had ever met with in any institution, and in the *viva voce* examination he had taken the highest value allotted to the answers. But something more striking was still to happen. At the close of the prize distribution Mr. Carteighe surprised the gathering by asking permission to say a few words in reference to the Pereira medal, and before the President had recovered from his surprise the young medalist proceeded to point out the weak points in the examination from which he had successfully emerged. This incident, trivial in itself, throws



an interesting sidelight on the character of this young student. In Carteighe's case it was not mere pushfulness that led him to forsake the beaten tracks of precedents; he felt that reform was needed, that this was the best opportunity for saying so, and he had the courage to take the opportunity. Before passing from this brief glimpse at Carteighe as a pupil, a word should be said as to his conduct as an apprentice. Mr. Radermacher, his old master, testifies to his punctual habits, his attention to instructions, his avidity for knowledge, and his anxiety to make the best use of his time. So from the beginning Michael Carteighe gave indications that much was expected of him, and in this he has not disappointed his old master, who has lived to witness the achievements of his apprentice, and is happily still with us.

In the year following the award of the Pereira medal, Mr. Carteighe was elected an auditor of the Pharmaceutical Society, and thus began an official connection with the Society which lasted without interruption up to the time of his death. Indeed, he attended the meeting of the Council on May 4 last and the meeting of the Library, Museum, School and House Committee on May 11. It was at the end of the year 1863 that he joined the firm of Dinneford and Co., of Bond Street, which was then carried on by his brother, John Carteighe and John Edward Stuart. The business became one of the best known in London, and here the energetic young pharmacist found scope for the application of much knowledge gained while at the School of Pharmacy. Three years later—in 1866—he became a member of the Council of the Pharmaceutical Society, as also a member of the Board of Examiners, but in 1869 a change was made in the By-laws which precluded anyone from filling the duties of Councillor and Examiner at the same time, and he withdrew from the Council, in order to serve the Society as an examiner. It was not until 1881 that he returned to the Council, but in this interval of eleven years he was closely associated with the Society, and performed many important and useful offices. He was the chief organizer of the first annual dinner of the members of the Society, which was held at the Crystal Palace in 1872, and he acted as Local Secretary to the London meeting of the British Pharmaceutical Conference in 1874. In the same year he gave evidence before a Select Committee of the House of Commons on the frivolous prosecutions which had been instituted under the Sale of Food and

Drugs Act, 1872. In 1880 and 1882 he was an honorary General Secretary of the British Pharmaceutical Conference, of which body he was Vice-President from 1883 to 1896. He was English Secretary of the Fifth International Pharmaceutical Congress, which was held in London in 1881, and at which he read a paper on "Pharmacopœia Revision," discussing therein the small share pharmacists had in the work. He came back to the Council of the Pharmaceutical Society in 1881, and in the following year was elected President, an office which he held uninterruptedly for a period of fourteen years.

That Mr. Carteighe was well equipped for the performance of the duties which the office of President involves has already been shown in the foregoing brief sketch of his career up to the time of his election as official head of the Society. But, in order that we may the better appreciate how well fitted he was to guide the destinies of the Society, it is necessary to go back to the year 1866, when he first became a member of the Council. That was at a time when the sale of poisons was under no legal restraint, and at a time when negotiations to secure legislation to place the practice of pharmacy on a regular basis began to come within the scope of practical politics. Carteighe was then a young man—he was, in fact, only twenty-five years old—and had only just been admitted to the counsels of the Society. Notwithstanding this, however, he was the confidant and adviser of Sandford, the then President, with whom he was in constant communication with reference to the pending legislation. The important part he played will never be divulged, for it was for the most part played behind the scenes, but this much we do know, that Mr. Carteighe did his utmost to prevent the insertion in the Bill of the words which became known as the Widow's Clause. He recognized that the position of chemists and druggists would be assailable if those words were inserted, so long as they remained. That his advice was right we learnt to our discomfort by the House of Lords decision in 1881, when, alas, it was too late for the knowledge to be of use. We are betraying no confidences in referring to these negotiations, for Mr. Carteighe himself, speaking at Manchester in 1895, pointed out that the 1880 judgment was due to the fact that in the Pharmacy Act of 1868 they had inserted a clause which differed from every other part of the Act. It began by asserting the necessity—for the safety of the public—

that every person who dispensed poisons should be qualified and registered and then immediately set to work to undo that by saying that, in the event of the death of a registered person, the qualification which was vested in his person should pass to executors, or his widow and children, provided a registered assistant were kept. The report of Mr. Carteighe's remarks on that occasion was as follows: "The insertion of that clause was a grave mistake. He and another member of the Council tried to exclude it from the draft Bill, but were unsuccessful. The Bill created on the one hand a sort of statutory professional title, which was to be purely personal in its character, and, on the other hand, tacked on to it something which simply applied to the conduct of a mere business which went like machinery. If chemists and druggists really believed that it was right and proper that their widows, administrators, or executors should have power to carry on business in the way now provided, it was hopeless and illogical to ask any legislature to deal with company traders."

By a singular coincidence the year in which Mr. Carteighe returned to the Council was the memorable year in which the House of Lords judgment confirmed the view which he had unsuccessfully endeavored to impress upon his colleagues in the years immediately preceding the legislation of 1868—to wit, that the position of chemists and druggists would be assailable always as long as the Widow's Clause remained. Under these circumstances it is natural to assume that Mr. Carteighe and his colleagues realized that the duty of the Society lay in the direction of removing the anomaly thus revealed. Several methods of obtaining this end suggested themselves. In the first place, there was the legislative method, and shortly after the decision the Council drafted a Bill to amend the Pharmacy Act of 1868. The Bill, commonly known as the "Omnibus Bill," contained sixteen clauses, one of which would have limited the period during which executors or trustees could carry on the business of a deceased chemist. The Bill would also have restricted the compounding of medical prescriptions to registered chemists, and have made employers liable for the acts of their assistants; while it was proposed that all duly registered persons should be exempted from serving on juries and inquests. It also provided that "in Section 12 of the Pharmacy Act, 1852, and also in Section 15 of the Pharmacy Act, 1868, the word 'person' shall include corporate bodies." This Bill

was never introduced into Parliament, for the reason that the Council's Parliamentary advisers showed conclusively that there was no prospect of proceeding with it successfully. Another Bill was drafted shortly afterwards, but never introduced, in which it was provided that in Section 12 of the Pharmacy Act, 1862, and in Section 15 of the Pharmacy Act, 1868, "words importing the masculine gender shall include the feminine gender, and words importing the singular shall include corporate bodies and the plural." In 1883, the second year of Mr. Carteighe's presidency, another Bill was drafted on similar lines; it contained twenty-three clauses, and shared the fate of its predecessors for a similar reason. So far as any attempt at legislation was concerned, matters were then allowed to remain in abeyance until 1887; when the measure of four clauses, which is usually known as the "Curriculum Bill," was produced, with the underlying idea that improvement of the status of the pharmacists by educational means was probably the best way of removing existing difficulties. That Bill was introduced into the House of Commons, and might have passed the second reading, but unfortunately none of those in charge of the measure were present when the opportunity presented itself for proceeding with the Bill. A fourth attempt was made in 1888, when a Bill was drafted in which it was again sought to secure powers to establish a curriculum. That Bill was introduced into the House of Lords by the Earl of Milltown; it passed through the Upper House, but did not get beyond its initial stage in the House of Commons. Another Bill dealing with education and the establishment of a curriculum was drafted in 1889, but it was not proceeded with owing to lack of support and the prevalence of the idea that it was not worth while to trouble Parliament about pharmaceutical education alone. A sixth Bill, promoted by the Council in 1890, contained a clause dealing with the proposed curriculum, and another restricting the dispensing of medicines to registered chemists. This was the measure on behalf of which Mr. Michael Carteighe endeavored to arouse enthusiasm by addressing meetings of chemists and druggists in various parts of Great Britain. He failed, however, to obtain any material support, and the Bill was not introduced into Parliament. A seventh Bill, on similar lines to that of the previous year, was drafted in 1891 and introduced into Parliament, but it was not fortunate enough to secure a second reading. Three years later another



Bill was proposed, with the two-fold object of admitting Associates of the Pharmaceutical Society to full membership and altering the procedure in connection with the retirement of members of Council. It was not proceeded with—again on account of lack of support—nor was a later Bill, drafted in 1895, which dealt with the same subjects and, in addition, proposed to restrict the compounding of medicines to chemists. That measure would also have given the Council power to erase names from the Register of Chemists and Druggists for infamous conduct in a professional respect, as well as to impose an annual fee for registration. Four years later, a Bill drafted with similar objects to that of 1894 received the Royal Assent, during the presidency of Mr. Walter Hills.

The Bills drafted during Mr. Carteighe's presidency by no means represented the whole of the work entailed in the endeavor to overcome the unfortunate difficulties which were shown by the judgment of 1880 to exist. It seemed hopeless to secure legislation to effect the desired purpose, and the Council turned its attention to the possibilities of litigation. The Council was engaged for a long period in the discussion of methods for dealing in the Law Courts with the defects revealed by the decision, the hope of arriving at a satisfactory remedy having doubtless been raised by some of the dicta of Lord Justice Blackburn. One of the results of these discussions was the institution of proceedings against the Leith Depôt, Limited, but the Society was unsuccessful, the High Court of Justiciary holding that the shareholders of a limited company are not personally liable under Section 15 of the Pharmacy Act, 1868.

Litigation and attempted legislation having failed, it remained for Mr. Carteighe to proceed with his own particular policy, the policy of improved education, with which his name will always be associated. No doubt there are many, even among Michael Carteighe's admirers, who still fail to see that his aspiration towards the higher education of pharmacists was engendered by a desire eventually to overcome the difficulties arising out of company trading. This was the case, however; he recognized before anyone else that until pharmacists were fitted by education to take their place among the professional classes, they would never obtain the privileges of those classes, and he set to work to bring the members of the craft to think as he thought. In this he was not wholly successful. Briefly put, Mr. Carteighe's idea was to raise the *status* of the

chemist and druggist, and thus place the Council in a position to ask Parliament for powers to erase from the Register the names of persons guilty of unprofessional conduct. In those days it would have been considered, without doubt, that a registered person who acted as cover to an unregistered person or a company would have been guilty of unprofessional conduct, but unfortunately the members of the craft had not the gift of seeing sufficiently far ahead, and so the policy in its fullest sense never matured. Nevertheless, his educational policy was not wasted, and to-day British pharmacists are reaping the benefit of it. Mr. Carteighe realized the force and the wisdom of the policy of the founders of the Society, namely, that the foundation of effective organization was education in its widest sense, and the major portion of his efforts were devoted to securing for the Society a *status* among recognized technical and scientific institutions of the country. He was successful in bringing the Society to the notice of a number of distinguished men, whose goodwill and co-operation were calculated to be of immense significance to a chartered Society. Among these may be mentioned the late Sir Michael Foster, Professor Dewar, Sir H. W. Acland, Sir Dyce Duckworth, Sir Henry Roscoe, Sir G. Sieveking, Sir Richard Quain, Sir Lauder Brunton, and Sir J. S. Burden-Sanderson. This was part and parcel of his policy to obtain recognition for the Society, by bodies whose influence would be of the utmost value.

Besides the Leith Dépôt case already referred to, the outstanding features of the legal work of the Society during Mr. Carteighe's period of office was a long series of important decisions. Thus it was shown by a judgment of the Queen's Bench Division that the use of the title "Shipping Druggists" by an unqualified person and a qualified person in association is an offence by the former. The word "Seller" within the meaning of Section 15 of the Act of 1868 was defined as the person who actually effects the sale. Proprietary preparations containing poison were shown, in the Piper case, not to be within the exemption of Section 16 (1868) relating to "Patent Medicines." It was held that the sale of a preparation containing poison is a sale of a poison. "Open shop" for the sale of poison was defined as a place where a poison may be purchased by the public. The use of the title "Chemist" was shown to be an offence in Scotland even when such title is associated with modifying words, and the words "Patent Medicines" in Section 16 of the

Act of 1868 were defined as medicines being the subject of Letters Patent in force. In the Piper case, as already mentioned, it was decided by the High Court in 1893 that proprietary medicines containing poison are not within the exemption of Section 16 relating to patent medicines. The Society found, however, that grants of Letters Patent for medicines containing poisons had been applied for with the object of evading the provisions of the Pharmacy Act, and although the Pharmaceutical Society had not the power to oppose the granting of such patents, Mr. Carteighe and the Council came to the conclusion that it was its duty to procure the revocation of such Letters Patent. The first case undertaken was in reference to a patent "for an improvement in cough mixtures," the patentee claiming "a preparation of hedge hyssop in conjunction with one or more ingredients therein described." Among the ingredients were morphine and chloroform, and on the Society's application an order for revocation was made. This case was followed by others, the Society almost invariably meeting with success in the campaign it had undertaken. This is a feature of Mr. Carteighe's period of office which most people may have forgotten, and is recalled to show how he endeavored in every possible way to perform the duties which he felt the Society owed to the public.

In *The Pharmaceutical Journal* Michael Carteighe took a very deep and constant interest. He was a frequent contributor to its pages during the period when the Journal was under the control of an Editorial Committee, and innumerable unsigned articles from his pen have appeared in these columns. It is interesting to note, by the way, that his first communication to the Journal was in 1862, when he directed attention to the fact that a weekly subscription had been commenced by the Associates and Students attending the lectures of the Society for the benefit of the Lancashire operatives who were suffering so severely from the failure of the cotton supply, and asking for subscriptions. *The Pharmaceutical Journal* was not the only publication of the Society in which he took a profound interest. His share in the production of the British Pharmaceutical Codex will probably be regarded, in the years to come, as being not the least important work of the strenuous life which he so largely devoted to the service of the Pharmaceutical Society and its School, for the good of pharmacy in general. Though the idea of the production by the Society of an authoritative formulary appears to have sug-

gested itself to Mr. Carteighe at an early period of his pharmaceutical career, many years elapsed before an opportunity of testing the practicability of any scheme based on that idea presented itself. Private interests blocked the way of progress, and there was a stern fight to wage against inertia, prejudice, and jealousy. Chance, however, provided the needed opportunity in the year 1903, when the judgment in the case of *Farmer v. Glyn-Jones* created a difficulty which, it seemed, could best be met by the publication, under the auspices of the Pharmaceutical Society, of a chemists' formulary of approved remedies. At the Council meeting in August of that year Mr. Carteighe proposed that a Compendium of Medicines in general use should be published by authority of the Council. It was pointed out by Mr. Carteighe that, apart from the British Pharmacopœia and the "Unofficial Formulary" of the British Pharmaceutical Conference, there was no authoritative work dealing with that enormous class of medicines known as domestic remedies. Moreover, it was urged, medical men and chemists and druggists knew less about the compounding of medicines than even they did, and the British Pharmacopœia was no guide to them. It was also insisted by Mr. Carteighe that medical men had not the time to learn how to prescribe properly, much less to learn how to compound medicines, nor was there any authoritative work on unofficial medicines to which they could refer for illustrations of what they ought to prescribe. Mr. Carteighe's motion was carried, a Committee appointed, the work set in hand, and the Codex published in October, 1907. It should be noted that the Council decided that the Codex should not consist solely of recipes for medicines, which, in accordance with the decision of the Inland Revenue with reference to the judgment already referred to, would become liable to medicine stamp duty after January 1, 1904. That was a special difficulty which required special treatment, and for that purpose "The Pharmaceutical Journal Formulary" was compiled, and it is important to note that it was mainly due to Mr. Carteighe's influence that this work was produced, as well as the Codex.

Apart from the anonymous articles already referred to, Mr. Carteighe did not contribute many scientific papers to pharmacy, the best known being the one he read at the British Pharmaceutical Conference at Exeter in 1869 on "Syrup of Iodide of Iron," and an article written for *The Pharmaceutical Journal* in March, 1871, on



"Syrup of Phosphate of Iron and other Syrups containing Phosphoric Acid." At Bristol, in 1873, he delivered a lecture, which was illustrated with experiments, on "The Diffusion and Occlusion of Gases," a lecture which showed his mastery of a difficult branch of physics. But it was his addresses on pharmaceutical politics by which the greater number of pharmacists will remember him. Some of his most brilliant efforts were made extemporaneously on occasions when no reporters were present to place his utterances on record. In speech he was a model of lucidity; he not only knew his subject thoroughly, but had the gift of presenting essential facts in such a way that his hearers not only understood what he intended, but carried away with them what he intended they should remember. His speeches expounded the policy which he consistently and persistently followed. He ever kept in view the main fact that Parliamentary and public recognition can never be accorded to the commercial side of the business of the chemist and druggist, and that protection of the professional side must be won by the exhibition of special fitness in the individuals who claim to work for the public safety. Hence the promotion of sounder education and technical training, the institution of research work, and the perfection of the machinery of examination, which must be forever identified with Mr. Carteighe's name. And hence, too, the metamorphosis in the School and its equipment, the foundation of the Research Laboratory, the development of the Journal, the Museum, and the Library, which earned for him the sobriquet of the "spendthrift President." But who shall say that the money was squandered? Surely not his successors, who have been enabled to harvest in many of the fields he has ploughed!

In 1893 he went to America with a number of members of the Council of the Society of Arts, which for the time being was constituted a Royal Commission for the organization of the British section at the Chicago World's Fair. Among Mr. Carteighe's colleagues on that occasion were Sir Richard Webster, the present Lord Alverstone (Lord Chief Justice of England), Mr. J. Fletcher Moulton, now Lord Justice Moulton, and other distinguished personages. While in Chicago he attended the forty-first meeting of the American Pharmaceutical Association, where he had a very cordial reception and addressed the members present, being introduced to the meeting by Professor Remington as a "gentleman who

is known all over the world in pharmaceutical circles." In this connection it is recorded that a most touching incident occurred when the President of the Pharmaceutical Society of Great Britain announced to the meeting that he was the bearer of the Hanbury Gold Medal which had been awarded to Professor Maisch for distinguished services and for original research in the natural history and chemistry of drugs. Though Professor Maisch was unable to be present at the meeting, this testimonial fortunately reached him while he was in full possession of his faculties, although suffering severely. His face, wasted by the long-continued pain to which he had been subjected, lit up with a smile of pleasure when he received it, but a few short days before his earthly existence closed.

In 1907 Mr. Carteighe left his Bond Street premises, and severed his long connection with the practice of pharmacy; this was a great wrench to him, an uprooting from old associations, which is at all times painful, and was particularly so to one of his temperament. Nevertheless, he continued to conduct his business affairs as usual, and attended the meetings of the Council of the Pharmaceutical Society with his accustomed regularity until the summer of 1908, when illness overcame him for a time, and left in its train the loss of the precious sense of sight, at first partially only, though later he heard us, but saw nothing. This great affliction was in a measure alleviated for a time by some improvement in Mr. Carteighe's general health; he continued to devote much attention to things that had formerly interested him and to allow his sense of benevolence to run riot, and in January last he returned to his work at 17 Bloomsbury Square. From that date until the end was very near he attended every meeting of the Council or Committees, astonishing everyone by his amazing display of energy and the acuteness of his intellect. Here, surely, we have the greatest example of his unflinching courage. Those around him saw—and sorrowed. He was invariably cheerful, though dependent upon the inflections of the voices of those around him to tell him what formerly he was wont to learn largely from their faces. He coupled with a courageous spirit an inexhaustible fund of benevolence, and to what extent it ran will never be told. When the cause of pharmacy required it, his time and purse were alike at its service, and he gave liberally from both. He was never too busy to help; he never turned anyone away empty.

The hopelessness of recounting in a single article a tithe of his services to pharmacy must be apparent to everyone who has followed Mr. Carteighe's career. He was devoted to the Pharmaceutical Society; his life was given unstintingly to its services. More especially is it a difficult task to appraise at its true value the character of one with whom it has been a privilege to labor. Perhaps the true keynote was struck in a character sketch of Mr. Carteighe by "An Old Admirer" which appeared in *The Pharmaceutical Journal* some five years ago. The writer said: "Mr. Carteighe will be known in history not so much for what he accomplished as for what he made possible of accomplishment. He had that attribute of the great man of which Landor speaks—the intellect which puts in motion the intellects of others. He was no rash innovator in politics, for he agreed that experimentalists, though perhaps the best philosophers, are always the worst politicians. With Diogenes in the 'Imaginary Conversations,' he inclined rather to teach chemists their duties, so they might know their interests. Opportunist to the finger-tips, he never took a mean advantage of the weakness of an opponent; vigorous to the verge of brutality, his tenderness to the sick or necessitous is unbounded; Homeric in his mirth, no nature ever responded more sympathetically to the grief of others. In short, a Man, with a rare combination of manly attributes and the concomitant faults common to erring mortals." We take leave of him with feelings of intense sadness and a sense of our irreparable loss. Much was expected of him; he was endowed with great physical and mental gifts, and out of his store he gave his very best to pharmacy.—*Pharm. Jour.*, June 4, 1910, pp. 699-702.

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## PHILADELPHIA COLLEGE OF PHARMACY.

### QUARTERLY MEETING, JUNE 27, 1910.

The quarterly meeting of the college was held in the library, at 4 P.M., the President, Howard B. French, presiding. Fourteen members were present. The minutes of the annual meeting held March 28th, were read and approved. The minutes of the Board of Trustees for April 5th, May 17th and 24th were read by the Registrar, Jacob S. Beetem, and after several minor corrections, were approved.

Prof. C. B. Lowe, for the Committee on Membership, reported

the changes in membership during the year, and made some suggestions regarding additional members.

Prof. S. P. Sadtler, for the Committee on Necrology, reported the names of deceased members as follows: Louis G. Bauer, M.D., died May 5, 1910, and he joined the college in 1869. David Jameson, died April 28., 1910, and he joined the college in 1871. David W. Ross, died May 17th, 1910, and he joined the college in 1879. George M. Beringer, Chairman, for the Committee on Centenary and Historical Committee, reported verbally that the Committees were keeping in view details of the work and would report progress.

Prof. S. P. Sadtler, for the Committee on Revision of the United States Pharmacopœia, reported verbally that a very full report of the proceedings of the convention had been published in the *AMERICAN JOURNAL OF PHARMACY* for June, 1910, pages 267-282, and he would mention but a few items. The college was, as usual, much in evidence in matters pharmaceutical. Sixteen of the graduates of the college were on the new Committee on Revision.

Prof. Henry Kraemer presented to the college a group picture of the late Committee on Revision, and a reproduction of a bronze-portrait tablet of the late Charles Rice, now in the New York College of Pharmacy. The thanks of the college were tendered the donor.

George M. Beringer, for the delegates to New Jersey Pharmaceutical Association, reported that the meeting was held at Cape May, N. J., June 14-17. This was the fortieth annual meeting of the oldest state pharmaceutical association in America. Mr. Edward A. Sayre, of Newark, presented an excellent historical address, describing a number of the important events in its history, and reviewing some of the problems and papers discussed during this period. Some seven or eight other papers were presented dealing with pharmaceutical subjects. A communication from the women's organization of the National Association of Retail Druggists directed attention to the distasteful methods of advertising certain wares sold by druggists. Resolutions were adopted strongly endorsing the attitude of the association, pledging the support of the members to suppress all forms of improper advertisements.

A special committee was appointed to draft a new pharmacy law to include a prerequisite clause, a proper definition of rural districts, and a revised schedule of poisons. The next meeting of the association will be held at Asbury Park.



O. W. Osterlund, for the delegates to the American Pharmaceutical Association, held at Richmond, Va., reported verbally that the meeting was largely attended. About three hundred members were in attendance, and a very instructive and enjoyable meeting was held. One of the very pleasant incidents of the meeting was a dinner of twenty-nine of the graduates of the Philadelphia College of Pharmacy, who were in attendance.

Prof. Henry Kraemer added that as a very full report of the meeting was published in the *AMERICAN JOURNAL OF PHARMACY*, June, 1910, pages 282-294, he would only mention the pleasure it gave him to be present at the dinner of the graduates of the college.

Prof. Henry Kraemer proposed the names of four gentlemen for honorary membership which, according to rule, were deferred to the next meeting of the college in September for action.

The President announced the following appointments:

Historical Committee (re-appointed): George M. Beringer, Henry Kraemer, W. H. Poley, Jacob M. Baer, and C. A. Weidemann.

Committee on Necrology: Henry Kraemer, S. P. Sadtler, and C. A. Weidemann.

Committee on Nominations: Joseph W. England, William E. Lee, William McIntyre, Charles H. LaWall, and H. C. Blair.

Prof. Henry Kraemer presented letters from two of our fellow-members for preservation in the historical collection—one from Feliciano Paterno, now a student at Berlin, and one from Manuel Zamora, a pharmacist in Manila.

The college went into executive session at 5.20 P.M. and remained in session till 5.45 P.M., after which it adjourned.

#### MINUTES OF THE BOARD OF TRUSTEES.

April 5. Nineteen members were present. George M. Beringer was elected Chairman, and Walter A. Rumsey, Vice Chairman. Jacob S. Beetem was re-elected Registrar. A communication from the Secretary of the college was read, giving the names of the officers and members of the Board of Trustees elected at the annual meeting of the college. The Committee on Library reported that they had engaged Mr. Mitchell Bernstein, Class of 1909, to act as temporary Librarian, his duties beginning on April 15th. Committee on Property reported that they authorized the purchase of a

vacuum cleaner for use of the college. Professor Sadtler referred to the work done in the library by Professor F. P. Stroup, who had devoted much time to the rearrangement of the library during the past few months, and moved that a vote of thanks be extended to him. Mr. French, in seconding the motion, expressed his appreciation of Professor Stroup's work. The motion was unanimously carried. The Committee on Appropriations presented their report, submitting the estimated amounts that would be needed for the ensuing year. Committee on Announcement moved that the matter of considering the merger of the Bulletin with the Alumni Report be referred to the Committee of Three, so ordered. The Chair appointed S. P. Sadtler, Joseph W. England, W. A. Rumsey.

The Special Committee on Athletics, which had been considering the advisability of establishing a Department of Physical Culture, made a lengthy report. After some discussion, and amendment, the report was adopted. The Department will be under the control of a Physical Director (preferably one having a medical degree) who will examine the students to determine the amount of physical exercise each one may require. Three members of the Board of Trustees, to be called the Sub-Committee on Physical Culture, will have charge and account for all funds appropriated for this Department.

The usual annual contribution was made to the Intercollegiate Department of the Young Men's Christian Association. Eta Chapter of Kappa Psi Fraternity requested the college to act as Trustee for such funds as they might raise for the purpose of securing a fraternity house. The Treasurer of the college was authorized to act as Trustee for their funds. A request for duplicate diplomas was received from Eugene Jacobs, '88, and H. O. Baer, '01, the originals having been destroyed. The request was granted, under the usual conditions. It was reported that the Wiegand Scholarship Fund amounted to \$3212.45. C. Mahlon Kline was elected to active membership.

May 3d. Owing to the absence of a large number of the Board attending the meeting of the American Pharmaceutical Association, no quorum was present, therefore, an adjournment was had, until May 17th.

May 17th. Sixteen members were present. The Treasurer presented his annual report. The Committee on Examinations reported the names of 105 candidates for the degree of Doctor in Pharmacy,

they having complied with all the requirements necessary for graduation; a ballot was taken, and they were duly passed, and it was directed that the degree of Doctor of Pharmacy be conferred upon them. The names of 15 candidates for the degree of Pharmaceutical Chemist were passed upon, and it was directed that the degree of Pharmaceutical Chemist be conferred upon them. The Chairman announced the names of those who were to present the prizes at the coming commencement. The Committee on Instruction presented the annual reports from the Faculty. Abstracts of their recommendations are given as follows:

Department of Pharmacy. Instruction in operative pharmacy was increased 40 per cent. during the year, and it is proposed to still further extend laboratory instruction, and arrangements were made to materially increase the facilities of the laboratories.

Department of Chemistry. It was recommended that during the first seven weeks of the course, that a fairly full outline of elementary physics be taken up, so as to better prepare the students for their chemical course. It was also recommended that an associate Professor of Chemistry be established, so as to relieve the present Professor (Samuel P. Sadtler) from some of his onerous duties, and Professor Freeman F. Stroup was appointed to the position.

Department of Botany and Pharmacognosy. The past college year in this Department has been one of the most satisfactory in the experience of the professor in charge. The third-year class has taken up the study of non-pharmacopœial drugs—especially those used in the formulas of the National Formulary. Great benefit has been derived from the botanical garden and the recently constructed greenhouse. The Jacobs-Maisch Botany prize has stimulated interest in the study of field botany.

The Committee on Examinations submitted a number of recommendations, which were disposed of as follows: The National Formulary together with the United States Pharmacopœia be designated as text-books in the several Departments of Instruction.

The thanks of the Board was tendered to the Lecturers in the Special Course held during the winter. Various other recommendations of the Committee on Instruction were referred to appropriate Committees.

Committee on Library reported that the work rearranging the library was progressing satisfactorily, under the care of the Acting Librarian.

Mr. H. B. Taylor presented to the college a copper mortar and

iron pestle over 100 years old, for which the thanks of the college were tendered the donor. A duplicate diploma was directed to be issued to W. A. Kulp, under the usual conditions.

May 24. Fourteen members present. Committee on Instruction presented a supplemental report. The resignation of E. L. Newcomb, Instructor in Department of Botany and Pharmacognosy, was accepted and the thanks of the Board was voted him for his faithful services. Professor Newcomb has accepted an appointment in another educational institution.

The recommendation that the results of mid-year and final examinations be sent to the parent or guardian of students, on request, was adopted.

The new roster was adopted, subject to such changes as the committee might direct.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

#### MAY PHARMACEUTICAL MEETING.

The last of the series of Pharmaceutical Meetings for 1909-'10 was held on Tuesday afternoon, May 24, at 3 o'clock. Mr. M. I. Wilbert, of the Hygienic Laboratory, Washington, D. C., presided.

The meeting was devoted entirely to the presentation of abstracts of their theses by some of the members of the graduating class of 1910. Specimens illustrating the results of their work were also shown. There was considerable discussion and the meeting proved to be of interest to all who attended.

The following students participated in the meeting: Peter Amsterdam, Samuel H. Bartholomew, Vastine A. Keister, Wallace E. Klopp, S. D. Lamb, Charles N. Lang, Donald A. McMillen, P. C. H. Webb.

As Professor Kraemer had previously stated that he desired to be relieved of the details and responsibilities of the work connected with the meetings (see this JOURNAL, May, 1910, p. 246) and as the By-Laws provide for the election annually of a secretary or recorder at the meeting in May, he accordingly recommended that Mr. Mitchell Bernstein, P.D., Acting Librarian, be elected to the office, stating that as Librarian he would be in a position to verify statements brought up in the discussion and prepare accurate accounts of the meetings for publication. Mr. Bernstein was then elected to the position of Recorder for the year 1910-1911.

HENRY KRAEMER,  
Secretary.



# THE AMERICAN JOURNAL OF PHARMACY

SEPTEMBER, 1910

## A NOTE ON THE ASSAY OF THE HALOGEN COM- POUNDS OF THE U. S. PHARMACOPŒIA, WITH SPECIAL REFERENCE TO THYMOL IODIDE.

BY ELIAS ELVOVE.

In connection with an investigation on the relative bactericidal value of the various embalming fluids on the market, which is now in progress in the Division of Pathology and Bacteriology of the Hygienic Laboratory, it was required, among other things, to examine a number of these fluids for the presence of chloral and to estimate its quantity wherever found. Owing to the more or less complex nature of these fluids and especially to the fact that nearly all of them contain comparatively large amounts of formaldehyde, the methods for estimating chloral, such as those given by Allen, Holland, or Schimpf, are inapplicable to these fluids. Thus Allen<sup>1</sup> gives the processes of Müller,<sup>2</sup> Wood,<sup>3</sup> and Meyer,<sup>4</sup> all of which depend on the reaction of chloral with alkalies with the separation of chloroform and measuring the volume of the latter. The smallest of the quantities of chloral operated on is 1 or 2 grammes (Meyer), while in the method of Wood 10 grammes are used, and in the method of Müller 25 grammes. In cases such as the embalming fluids under consideration, where we may be dealing with comparatively small quantities of chloral, this circumstance alone would bar consideration of any method which

<sup>1</sup> Allen: Commercial Organic Analysis, 3rd ed., Vol 1, pp. 229-230.

<sup>2</sup> *Zeit. f. Chem.*, (2), 7, 66, and *Jour. Chem. Soc.*, 24, 444.

<sup>3</sup> *Pharm. Jour.*, (3), 1, 703.

<sup>4</sup> Meyer (and Haffter): *Ber.*, 6, 600-601, and *Jour. Chem. Soc.*, 26, 1163.

is based on measuring the volume of chloroform produced. According to Holland,<sup>5</sup> chloral is estimated by adding a measured amount of  $\frac{N}{1}$  NaOH to render the solution distinctly alkaline and determining the excess of alkali (Meyer's method). Schimpf<sup>6</sup> gives essentially the same method, but also includes the iodometric method of Rupp.<sup>7</sup> However, neither the alkalimetric nor the iodometric method is applicable to the estimation of chloral in the embalming fluids on account of the simultaneous presence of formaldehyde.

Fortunately, the fact that chloral contains chlorine, which can be converted into a chloride, affords a simple and convenient basis for indirectly estimating the amount of chloral. Procedures for decomposing the organic molecule so as to obtain its chlorine in the form of chloride are given by many authors under chloroform, but under chloral preference appears to be given to some form of the alkalimetric method, while a number of authors even omit any reference to the chloride process in the latter case. That such preference is not justifiable, however, may be seen from the work of Hinrichs,<sup>8</sup> who has pointed out the gross errors (varying from 180 to 200 per cent.) resulting from the alkalimetric procedure when the term "heating," as used by the British Pharmacopœia, is taken to mean warming till all the odor of chloroform has disappeared. Hinrichs, therefore, describes a modification of that method which, however, still does not make it suitable in the case of the embalming fluids; so that for general analytical purposes the chloride method is probably the best of all.

This chloride method may be carried out according to either the procedure of Wallis<sup>9</sup> or that of Self.<sup>10</sup> The essential feature of Wallis' procedure is the decomposition of the chloral by heating with an alcoholic solution of alkali under pressure, which is effected by heating the mixture in a closed bottle by means of boiling water for three hours. This is, therefore, practically the same procedure as that previously described by Puckner<sup>11</sup> for the estimation of chloroform. In Self's method the decomposition of the chloral is effected by boiling the solution containing the chloral with zinc

<sup>5</sup> Holland: *Medical Chemistry and Toxicology*, 2d ed., p. 412 (1908).

<sup>6</sup> Schimpf: *Manual of Volumetric Analysis*, 5th ed., pp. 647-8 (1909).

<sup>7</sup> *Arch. Pharm.*, **241**, 326-8 (1903), and *Jour. Chem. Soc.*, **84**, (2), 699 (1903).

<sup>8</sup> *Pharm. Jour.*, (4), **16**, 530-532 (1903).

<sup>9</sup> *Pharm. Jour.*, (4), **22**, 162-163 (1906).

<sup>10</sup> *Pharm. Jour.*, (4), **25**, 4-7 (1907).

<sup>11</sup> *Proc. A. Ph. A.*, **49**, 294-297 (1901).

dust under a reflux condenser, the zinc dust being replaceable by zinc filings and acetic acid, or by aluminium powder and acetic acid, the time required for effecting the decomposition of the chloral in Self's procedure being only from twenty to thirty minutes.

In this connection it seemed to the writer that having such excellent methods for estimating chloral and chloroform, it would be desirable that the U. S. Pharmacopœia (which at present gives no method whatever for estimating the percentage purity of these substances, although in the case of chloroform it prescribes a purity of 99 to 99.4 per cent.) should include, in the next revision, methods of assay based on these principles. Such want should be filled not only for the sake of consistency and completeness, but also because there is actual demand for such methods, as may be seen from the fact that the British Pharmacopœia had included a method for assaying chloral hydrate even before either Wallis or Self described their improved (chloride) methods and although the B.P. procedure, as already mentioned above, was shown by Hinrichs to be very far from satisfactory. Similarly, Gane and Webster<sup>12</sup> cite a controversy with one of the large users of iodoform as showing the importance of establishing a standard method of assay for this substance and point out that Utz's<sup>13</sup> method might be used, wherein the iodine of the iodoform is converted into silver iodide and the excess silver nitrate determined volumetrically. Likewise, in the case of bromoform (for which the present U.S.P. prescribes a purity of 99 per cent. without, however, giving any method of assay), Richaud<sup>14</sup> has pointed out how its bromine can be readily converted into bromide and the bromoform thus estimated through a determination of the resulting bromide. In other words, there appears no sufficient reason why a number of the halogen-containing substances of the U.S.P. should remain without any method of assay when it is quite probable that every one of them could be very readily estimated through a determination of its halogen. Further, it is quite probable that the conversion of the organic halogen into inorganic halide can be effected in all cases by some modification of the alkaline or of the reduction method (typified by the Wallis and Self procedures, respectively,

<sup>12</sup> *Pharm. Jour.*, (4), 28, 555 (1909).

<sup>13</sup> *Apoth. Zeit.* (Berlin), 18, 869 (1903).

<sup>14</sup> *Jour. de pharm. et de chim.*, (6), 9, 232-236 (1899), and *Jour. Chem. Soc.*, 75, (2), 527 (1899).

in the case of chloral) or through a suitable combination of these. The basis of all these assays would be the Volhard method, which is already in the U.S.P., but which is not fully utilized even where it is directly applicable. Moreover, the Volhard method might be applied to a number of other U.S.P. substances by previously introducing halogen into them, as was pointed out by the writer<sup>15</sup> in the case of a large number of the alkaloids. It will be seen, therefore, that while we would thus supply methods of assay where none are given at present, we would at the same time not increase the requirements for analytical skill on the part of the pharmacist, but simply extend the usefulness of a well-known method (the Volhard method) which is very easily carried out and which might be made to cover a very large portion of the U.S.P. field.

It appeared from the literature examined that thymol iodide,  $(C_6H_2.CH_3.C_3H_7.OI)_2$ , is especially difficult to decompose by a wet process so as to convert its halogen quantitatively into inorganic (or readily ionized) iodide. Thus according to Gane and Webster<sup>16</sup> "none of the usual wet methods is applicable; only partial decomposition is effected by heating with alcoholic potash to 130° C. under pressure, while neither treatment with silver nitrate and nitric acid nor with freshly precipitated silver chloride is suitable." Owing to this, "resort was therefore had to fusion with alkali carbonates." To carry out such fusion, 1 Gm. of the thymol iodide is intimately mixed with an equal amount of  $KNaC_4H_4O_6$  and 5 Gms. anhydrous  $Na_2CO_3$ . A porcelain crucible of 30 c.c. capacity is used, and a mixture of 1 Gm.  $KNaC_4H_4O_6$  and 5 Gms. anhydrous  $Na_2CO_3$  is employed to cover the mixture containing the thymol iodide. It is directed to "heat to such temperature as will ensure production of a perfectly white fused mass in forty-five minutes." After cooling, "thoroughly extract the fused mass with water," filter, and determine the halogen in the filtrate. As stated by these authors, resort was had to the fusion method only after finding the usual wet methods unsuitable. Inasmuch, however, as Gane and Webster apparently had not tried the reduction method, it was thought desirable to make some trials with the latter method. The following experiments were therefore carried out.

<sup>15</sup> Bull. No. 54, Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv., Wash., and *Jour. Amer. Chem. Soc.*, **32**, 132-139 (1910).

<sup>16</sup> *Drug Topics*, **24**, 52-53 (1909).



# GENERAL MODE OF PROCEDURE.

As a result of some preliminary experiments, it was found that the following procedure yielded satisfactory results: The thymol iodide<sup>17</sup> (0.1 to 0.5 Gm.) was treated, in a 500 c.c. Erlenmeyer flask, with 10 c.c. of ether (U.S.P.), followed by 20 c.c. of approximately  $\frac{N}{2}$  alcoholic<sup>18</sup> sodium hydroxide and 2 Gms. zinc dust,<sup>19</sup> mixing thoroughly after adding each of these constituents. The contents of the flask were then actively boiled under a reflux condenser for one hour. The flask was then disconnected from the condenser and the contents acidified with 10 c.c. of glacial acetic acid (99.5 per cent.) and diluted with 200 c.c. of distilled water, mixing thoroughly after adding each of these constituents. The contents of the flask were then again actively boiled under the reflux condenser for another hour. (With this procedure there is the fortunate circumstance that the undissolved residue tends to conglomerate, while the liquid finally becomes perfectly clear and hence filters very rapidly.) The condenser was then washed with a small amount (about 10 c.c.) of water which was allowed to drain into the flask and the contents of the latter filtered (using about 30 c.c. of hot water in the washings). The filtrate then received a measured amount of  $\frac{N}{10}$  AgNO<sub>3</sub> which was a little (about 5 c.c.) in excess of that theoretically required. The whole was then actively boiled for ten minutes, 50 c.c. of dilute (10 per cent.) nitric acid added, and again actively boiled for five minutes. After filtering (using about 30 c.c. of hot water in the washings) and cooling to room-temperature, the excess silver in the filtrate was determined by means of standard thiocyanate, using 5 c.c. of 10 per cent. ferric alum as indicator.

In applying the above method to assaying thymol iodide, it should also be possible to determine any considerable amount of chlorine, if present, by weighing the silver precipitate and finding the amount of chlorine by calculation as pointed out by Gane and Webster.<sup>20</sup>

In order to determine the effect of varying the time of the

<sup>17</sup> The thymol iodide used in this work was obtained from a well-known firm whose products usually are of a high degree of purity.

<sup>18</sup> Prepared by dissolving 20 Gms. of NaOH in 40 c.c. water and making up to 1000 c.c. with alcohol (U.S.P.).

<sup>19</sup> As zinc dust frequently contains small amounts of chlorine suitable controls were made in all cases.

<sup>20</sup> *Loc. cit.*

alkaline or the acid boiling, experiments were carried out in which the boiling time of one remained constant (one hour), while the boiling time of the other varied (up to three hours). The results obtained are given in the accompanying tables.

TABLE I  
*Effect of Varying the Time of the Acid Boiling*

No. of experiment	Amount of thymol iodide	Time of alkaline boiling	Time of acid boiling	$\frac{N}{10}$ AgNO <sub>3</sub> required	Apparent iodine content
	<i>Gm.</i>	<i>Min.</i>	<i>Min.</i>	<i>c.c.</i>	<i>Percent.</i>
1.....	0.3	60	15	10.62	44.93
2.....	0.3	60	30	10.68	45.18
3.....	0.3	60	45	10.70	45.27
4.....	0.3	60	60	10.58	44.76
5.....	0.3	60	120	10.70	45.27
6.....	0.3	60	180	10.70	45.27

TABLE II  
*Effect of Varying the Time of the Alkaline Boiling*

No. of experiment	Amount of thymol iodide	Time of alkaline boiling	Time of acid boiling	$\frac{N}{10}$ AgNO <sub>3</sub> required	Apparent iodine content
	<i>Gm.</i>	<i>Min.</i>	<i>Min.</i>	<i>c.c.</i>	<i>Percent.</i>
1.....	0.3	0	60	5.35	22.63
2.....	0.3	15	60	10.00	42.31
3.....	0.3	30	60	10.52	44.51
4.....	0.3	45	60	10.70	45.27
5.....	0.3	60	60	10.65	45.06
6.....	0.3	120	60	10.72	45.35
7.....	0.3	180	60	10.77	45.56

TABLE III  
*Effect of Varying the Amount of Thymol Iodide*

Time of alkaline boiling: One hour.

Time of acid boiling: One hour.

No. of experiment	Amount of thymol iodide	$\frac{N}{10}$ AgNO <sub>3</sub> required	Apparent iodine content
	<i>Gm.</i>	<i>c.c.</i>	<i>Percent.</i>
1.....	0.1	3.57	45.31
2.....	0.2	7.15	45.37
3.....	0.3	10.60	44.85
4.....	0.4	14.35	45.53
5.....	0.5	17.87	45.36

Percentage of iodine in thymol iodide, according to U.S.P. .... 45.00  
 Apparent iodine content as found by fusion method (similar to that  
 of Gane and Webster) ..... 44.52

The following result was obtained by the above-described procedure in working with an ether-alcoholic sodium hydroxide mixture containing some of the thymol iodide used in this work, the amount of which was unknown to the writer at the time of working with it, having been prepared by Dr. Norman Roberts of this laboratory and submitted to the writer as an "unknown."

Amount of thymol iodide given	$\frac{N}{10}$ AgNO <sub>3</sub> found to require	$\frac{N}{10}$ AgNO <sub>3</sub> as calculated <sup>21</sup>	Apparent iodine content
Gm. 0.4751	c.c. 16.88	c.c. 16.95	Percent. 45.09

From these results it would seem that a period of one hour for the alkaline boiling and another hour for the acid boiling should be sufficient for most practical purposes even when employing as much as 0.5 Gm. of the thymol iodide, which appears to be a suitable amount to take for the assay.

PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.  
 HYGIENIC LABORATORY, WASHINGTON, D.C.

<sup>21</sup> This calculation is based on the average value of the thymol iodide in terms of the  $\frac{N}{10}$  AgNO<sub>3</sub> as shown by the results given in Table III.

## ERGOXANTHEIN.

ERGOXANTHEIN, A NEW ACTIVE PRINCIPLE FOUND IN ERGOT, WITH  
A BRIEF HISTORICAL SUMMARY OF THE DISCOVERY OF  
THE ALKALOIDS OF ERGOT.

BY W. T. WENZEL.

The writer has nothing further to announce on the alkaloids ecboline and ergotine, the discovery of which has been duly credited and confirmed by numerous investigators at home and abroad. Their discovery was announced in this JOURNAL in 1864 (*AM. JOURN. PHARM.*).

However, the priority as to the naming of these alkaloids has been ignored by Kobert, in 1884, in changing the name of ecboline to coruntine, by Barger, in (1907) changing it to ergotoxine, and by Tanret, in 1875, ergotine to ergotinine. Ecboline, the name selected by the writer, is from the Greek word *εκβολη*, the literal translation of which is "to throw out," or expel. No word could have been better chosen or adapted, on account of the physiological action of this alkaloid, the producer of the tonic contraction of the uterus.

Barger and Dale make the statement in their publication (*Ergotoxine and Constituents of Ergot*) as a matter of fact that ergotoxine (ecboline) in intact pregnancy of cats, as well as post-partem cases, causes uterine contractions.

Kobert admitted that ecboline and coruntine were identical (*Ueber die Bestandtheile und Wirkungen des Mutterkorns* 1884, p. 46), but said that it was a very impure substance or preparation of his alkaloid, which he obtained by shaking out of alkaline solutions by acetic ether.

(I make this statement that Dragendorff's method of extraction of organic principles from immiscible liquids by ether was not known in 1864.)

Kobert also changed the name of sclerotinic acid, another constituent of ergot, discovered by Dragendorff and Podwyssotzki (1876), into ergotinic acid, and the only reason he gave for making this change was that his ergotinic acid was the purer.

Usually, claims of priority of discovery rest with the discoverer, and such rights should be respected.

"Honor to whom honor is due" and much honor is also un-



questionably due to Kobert, Barger, Dale, and others, for the amount of labor bestowed to obtain the valuable results in elucidating the chemistry and physiologic action of the active constituents of ergot.

The writer, herewith, announces an active constituent found in the fluidextract of ergot, not an alkaloid, but a principle possessing an undoubted action upon the human organism. This substance has been provisionally named *ergoxanthëin* (ergot-yellow) on account of the color of its alcoholic and ethereal solutions.

#### THE PREPARATION OF ERGOXANTHËIN.

Twenty-five cubic centimetres of Squibb's fluidextract were mixed with 75 c.c. of 95 per cent. alcohol, the mixture allowed to stand, with occasional shaking, about 12 hours. A dark brown precipitate will separate out, the clear supernatant liquid acquiring a sherry-wine color.

The precipitate is composed principally of Dragendorff's scleromucin, a violet coloring matter probably scleroxanthin, a resin, and magnesium, potassium, and iron salts of phosphoric acid.

The filtrate from this precipitate was evaporated in a shallow dish at a temperature of about 30° C. until the alcohol was completely expelled, adding from time to time water. Then diluted with water to measure 50 c.c., allowed the mixture to cool, and the dark brown precipitate to settle. Next transferred the mixture to a filter, collected the precipitate and washed it with water until 100 c.c. of filtrate were obtained. This brown precipitate represents the impure sphacelic acid of Kobert mixed with separated carbon.

The filtrate from this precipitate was then transferred to a stoppered separator, mixed with an equal volume of chloroform, and well shaken together, in order to remove a resinous substance. The filtrate having been shaken out thoroughly by chloroform was next mixed with an equal volume of ether and shaken until the ethereal extraction became nearly colorless.

The shaking out in each case should be continued at least three times. The mixed ethereal yellow extraction which now holds the *ergoxanthëin* in solution was distilled from a Liebig's condenser to a small volume, transferred to a small tared beaker, the liquid finally evaporated on a water bath to dryness and weighed. The amount of *ergoxanthëin* usually obtained will average about 0.25 per cent.

This solid residue when dissolved in 25 c.c. of alcohol will constitute the standard solution, representing 25 c.c. of the fluidextract, to be used in the physiologic and spectroscopic experiments.

#### PHYSICAL AND CHEMICAL PROPERTIES.

Ergoxantheïn presents an orange-yellow, uncrystallizable solid. It is soluble in alcohol and ether, but insoluble in water and chloroform. Its alcoholic solution does not redden blue litmus paper. It combines with alkaline bases forming blood-red solutions, alcoholic or aqueous.

Ergoxantheïn seems to bear a close relationship to luteïn, a yellow resinous pigment distributed in the vegetable and animal kingdom. Luteïn is a constituent of the ray-fungus, the spectrum of which is almost identical with that of ergoxantheïn, but it differs materially in its behavior towards chemical tests.

When solid ergoxantheïn is brought in contact with strong nitric acid, its yellow color is changed to a deep orange color, while luteïn acquires a blue color. Sulphuric acid dissolves ergoxantheïn to a blood-red solution. These substances also differ in the color of their solutions in chloroform, luteïn giving an orange color, while ergoxantheïn retains its yellow. Again, ergoxantheïn is very soluble in alcohol, on the other hand, luteïn is sparingly soluble and in concentrated hot solutions deposits orange flakes on cooling.

Ergoxantheïn is soluble in ether, benzene, acetic ether, amyl alcohol, acetone, and carbon disulphide. Insoluble in water, carbon tetrachloride and chloroform.

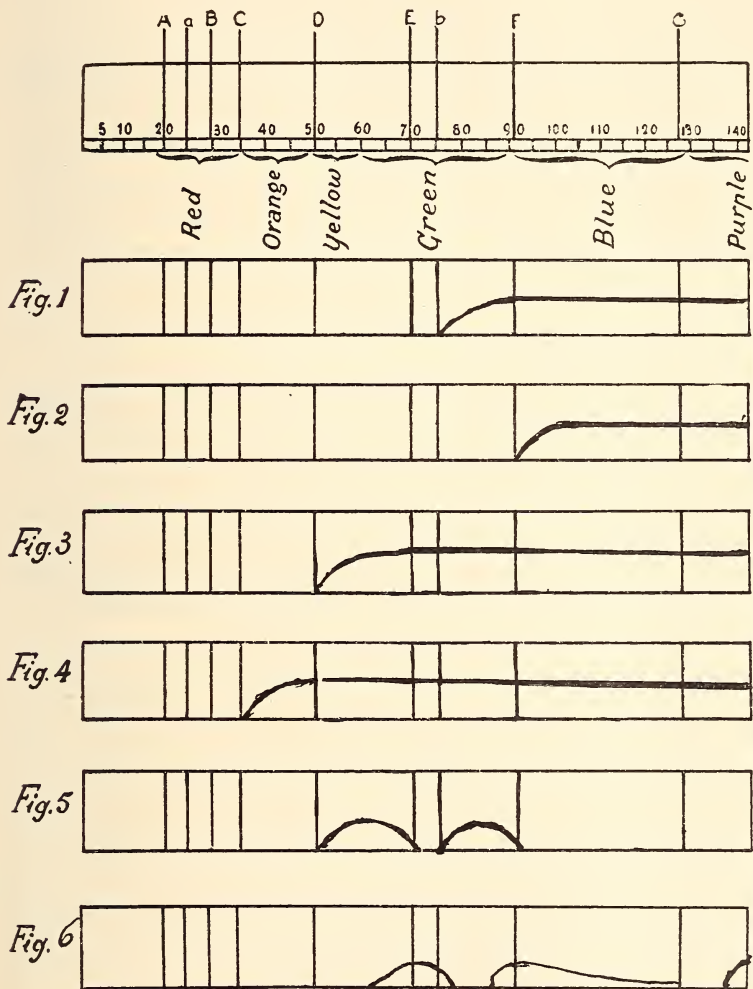
Basic lead acetate precipitates it from alcoholic solutions as an orange precipitate. It is not precipitated by barium chloride. Phosphotungstic acid precipitates ergoxantheïn yellow.

#### ON OTHER PIGMENTS FOUND IN ERGOT.

Zinnin, in 1853, showed that a coloring matter could be extracted from ergot by means of alcohol strongly acidulated with sulphuric acid. He recommended it for the detection of ergot in flour. But no spectrum analysis of it was made.

Uffelmann announced (*Archiv. f. Hygiene, Jahresbericht der Pharm.*, 1881-82) a yellow coloring matter, which he also proposed as a test for the presence of ergot in flour, by the extraction with a weak solution of caustic soda. The red liquid which he obtained

was acidulated with hydrochloric acid which changed it to a rose color. This liquid when shaken out with ether, and this solution subjected to spectrum analysis gave the spectrum, Fig. 5.



Absorption spectra of solutions of ergoxantheïn and other substances.

Wladimir Tichomirow proposed (*Pharm. Zeit. für Russland*, 1865) the spectrum, shown in Fig. 6, of another pigment for the discovery of ergot in flour, as in Zinnin's case a blood-red solution

was obtained on extracting the suspected flour with alcohol, strongly acidulated with sulphuric acid. Evidently, this pigment was identical with that of Zinnin's.

Fig. 1.—This spectrum represents the absorption spectrum of lutein existing in the ray-fungus, *Actinomyces* (pathogenic).

Its absorption beginning at the Fraunhofer line b. and continuing to the end, showing an absorption of a part of the green, the blue, and purple luminous rays (strength of solution unknown).

Fig. 2.—This represents the spectrum of ergoxanthëin solution as it appears in the 25 c.c. as obtained from 25 c.c. of the fluid-extract which also represents the standard solution as previously stated contained in a test-tube having an internal diameter of 10 mm. The absorption will be seen to commence at the line of F., and continue to the end. It will be seen that this absorption is less than that of the preceding.

Fig. 3.—This gives the spectrum of an alcoholic solution of ergoxanthëin made strongly alkaline with ammonia, which has changed its yellow to a blood red. This spectrum shows its absorption to begin at the D. line leaving intact the orange and the red.

Fig. 4.—This absorption spectrum represents the preceding ammoniacal solution of ergoxanthëin viewed through a 100 mm. sugar tube filled with this solution. By means of this arrangement all of the colors of the spectrum are eliminated with the exception of the red, the absorption beginning at the C. line.

In diluting this normal alkaline alcoholic solution of ergoxanthëin, in the proportion of 2 c.c. to make up 10 c.c. solution, and analyzing the same by the spectroscope through the 200 mm. tube, a spectrum will be obtained identical with that of Fig. 4. From this we may infer that the spectrum analysis of a solution of ergoxanthëin representing equal volumes of it and that of the fluidextract may not only be of value in forensic chemical analysis, but also be useful in a quantitative determination of ergot in preparations containing ergot or its fluidextract. Since by such colorimetric method, through a 200 mm. sugar tube two-fifths of a cubic centimetre of a fluidextract equal to 0.4 Gm. of ergot may thus be estimated.

Fig. 5.—The spectrum of Uffelmann's yellow coloring matter showing an absorption band between the Fraunhofer line C. and E. and another band between the line B. and F.

Fig. 6 gives the spectrum of Tichomirow's pigment which, as will be seen, differs materially from the preceding spectra. Its



appearance is that shown in dilute solutions; in concentrated solutions the absorption is complete from the D. line to the end.

In connection with this subject it should be stated that Dragendorff and Podwyssotzki's scleroxanthëin, fusco sclerotinic acid scleroerithrin, and sclerojodin belong to the analogous series of ergot pigments. They are characterized by forming color-combinations with alkalies. They are with the exception of scleroxanthëin soluble in strong alcohol only, and therefore do not appear as constituents of the official fluidextract on account of their insolubility in the menstruum used in its preparation: scleroxanthëin being the exception. As the following data will show scleroxanthëin and ergoxanthëin have nothing in common.

Scleroxanthëin is a crystalline substance. It is soluble in alcohol, and soluble in water. When its solution is treated with ferric chloride it is first colored violet, then changed to blood red.

On the other hand, ergoxanthëin is very soluble in alcohol, but insoluble in water. When its solution is treated with ferric chloride, instead of violet or red, the yellow color is changed to a dark amber.

#### ON THE PHYSIOLOGIC ACTION OF ERGOXANTHËIN.

For ascertaining the action of ergoxanthëin upon the human organism the standard alcoholic solution of 25 c.c., equivalent to 25 c.c. of the fluidextract, was used. Of this solution 1 fluidrachm, equivalent to about 4 c.c., was used as a dose for determining the blood-pressure by Gaetner's Tonometre, Dr. A. W. Perry, San Fran., officiating. The pressure was recorded in millimetres taking also at the same time the pulse beats of the radial artery. The observations were made every 5 minutes. After ten minutes, the pulse dropped from 80 to 75 beats per minute. The blood-pressure at the initial point stood at 133 mm., had now risen to 168 mm. as its maximum pressure, giving an increase of 27 mm. The blood-pressure from this time on dropped to its initial within half an hour, the slowing of the blood beats during the experiment being the general law that the lowering of the pulse is inversely proportional to the blood-pressure.

The following effects were experienced by the writer during the experiment:

A sense of fulness in the head, face flushed, considerable mental exhilaration.

This experiment was repeated several times, with slightly varying results.

Additionally, it may be asked why the author selected the official fluidextract of ergot for the foregoing investigation; it may be stated, that I have been prompted by several reasons. *First*, a promise that I would present a paper to be read at the meeting of the American Pharmaceutical Association, held in Los Angeles, on the "Quantitative Estimation of the Alkaloids Ecbo-line, and Ergotine in the Official Fluid Extract of Ergot."

During the course of analysis, when finally the chloroform solution was evaporated spontaneously, the ergotine was found to occupy the centre of the deposit in the form of prisms, while the amorphous ecbo-line occupied the peripheral margin of the deposit.

In order to separate the two alkaloids by the usual solvents in which they were both readily dissolved, carbon tetrachloride seemed to dissolve ergotine in preference to ecbo-line, but, unfortunately, it dissolved also a portion of ecbo-line thus rendering the complete separation of the two alkaloids so far hopeless, and the result, for the present, must remain *in statu quo*.

*Second*, having at this time the fluidextract under investigation, I desired to make, also to institute, a systematic qualitative analysis of it believing that inasmuch as Squibb's fluidextract prepared by repercolation would fully represent the medicinal activity of the drug, naturally, preference was given to it.

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## MANUFACTURE OF MEDICINAL PLASTERS.

BY FREDERICK B. KILMER.

I understand that Professor Remington is authority for the statement that the spreading of plasters has, to a great extent, become a lost art to the pharmacists of this country. If this statement be accepted it may be well for a few moments to go back into history in order to obtain some information in regard to this so-called "lost art."

We are told that the art of surgery had its birth at the time when injuries of primitive man began to be bound with adhesive substances made from the gums and juices of the forest. We know that as an accompaniment to the incantations of the medicine man use was made of the poultice or plaster, which, though empirical, had

some beneficial action. From the priesthood of Isis down to the monks of the near past, we find a remarkable knowledge of gums, juices, resins, and that remedial applications of plasters, salves, and ointments were skilfully prepared therefrom. In the *Materia Medica* of the Aryans, we find that they gave particular attention to the preparation of ointments, salves, plasters, and poultices. The Greeks assigned a place within their temples, where plasters were spread and medicines prepared by trained pharmacists. From the writings of Moses and from Egyptology we find that the Egyptians had a skilful knowledge of gums, resins, ointments, salves, blisters, etc., and knew how to apply them. In the plaster dispensed by the Chinese pharmacist of to-day, we look upon the form of plaster in use at least as far back as the middle ages. A novel method of plaster making is of ancient Arabic origin. It seems that certain kinds of domestic wines are treated with pitch, which gives to them a decidedly smoky flavor. This wine is stored or carried about in leather bottles. In the course of time the interior of the container is coated with the deposited pitch and wine sediments. The leather bottle is then cut into plasters, which find a ready sale. Many formulas found in the pharmacopœias of the present day, including those of plasters, are modifications of similar ones which descended from Hippocrates, Herophilus, and Mantras, who lived in periods ranging from 250 to 500 years, B.C. One branch of the so-called "sects" who controlled medicine about 300 B.C. relied largely upon the use of narcotics, such as opium, conium, and hyoscyamus, in their plaster and poultice making. The well-known diachylon plaster is quite similar to one devised by Menecrates, who lived in the first year of the Christian Era. In the first authoritative guide, or pharmacopœia, viz., that of Valerius Cordus, the formulas for plasters included a large proportion of diachylon base, with which he incorporated vegetable and mineral drugs, plant juices, etc. Many of the pharmacopœial plasters of the present time are evolutions of those given by this author. As Menecrates compiled and put into intelligent form the formulas of the schools preceding him, we can believe that many of our official formulas have the merit of antiquity.

That the condition of the drug trade, especially as applied to plasters, has not greatly changed may be deduced from a memorial of the druggists of Nuremberg, in 1581, who recite, among other things, that—"Counter sales are now made by the cheap corner

grocery shops, thus robbing the druggist of a source of profit that he is justly entitled to. Ointments and plasters, which certainly belong to the exclusive field of pharmacy, are now dispensed by barbers and physicians, who are neither justified by precedent nor by qualification to handle these things."

In our own country there is evidence of an ancient and advanced civilization which existed on some parts of the continent, and among the relics of this ancient civilization are implements of pharmacy. It has been suggested that the Pueblo Indians, who are descended from the Aztecs, have from a remote time made plasters, salves, and cerates, which they sometimes spread on skins, leaves, and flexible barks, and it is believed that they knew the art of applying them in surgery.

The early colonists derived a great amount of medical knowledge from the Indians, and the gums of the new-found world were early made articles of commerce in the shape of salves, plasters, etc., which were lauded as "new discoveries" possessing miraculous virtues. Many a colonial quack gained his reputation on the supposed merits of his "wonderful healing plasters," and at times these were sent back to the old country. An early American industry, conducted by the Huguenots, was the preparation and tanning of skins for the use of the plaster makers of France.

In the early days of medical practice in this country the plasters were made in the doctor's office by the apprentice, or by members of the family of the practitioner. Colonial merchants handled in considerable quantities, plasters in sticks, rolls, and spread plasters, the mass for which was imported. These were mainly diachylon and epispastic plasters. Blister plasters were evidently popular in colonial days. In one physician's bill, noted by the writer, blister plasters were charged to the same patient twenty-six times in two months, the average price for these plasters was three shillings.

From the colonial days until about 1874, the pharmacopœial plasters were made up almost entirely with the diachylon base. There are probably pharmacists who are familiar with the once well-known names of De La Cour, Wyeth, Maxwell, Shoemaker, Ellis, Skidmore, Shivers, and Husband as plaster manufacturers. These makers produced plasters in rolls to be spread by the pharmacist, or which were spread upon kid, sheepskin, or cloth. Products of this character were in common use as late as twenty-five years ago.



The manufacture of De La Cour's adhesive plaster is associated with Philadelphia in the present generation with Joseph Carl De La Cour, a graduate of the Philadelphia College. The original maker was John Charles De La Cour, who was an apprentice in a drug store in Philadelphia. He opened a drug store in Camden as early as 1836. It is stated that at this time this was the only drug store in New Jersey, south of Bordentown. He became a manufacturer and prepared solid and liquid preparations, old-fashioned court-plaster, and a general line of pharmaceutical preparations. He was among the earliest producers of ready spread or machine spread adhesive plaster in this country; he improved the formula of what is known as De La Cour's improved adhesive plaster, which was extensively used in hospitals and in the army and navy of the United States. It also became popular in tropical countries and in these countries has a large sale to-day. The manufacture is still continued in the laboratories by the original process, under the supervision of J. Carl De La Cour.

There are probably a number remaining in the ranks of pharmacy who have a vivid recollection of plaster making as practised a little over a generation ago. Plaster spreading was directed to be done with the aid "of a peculiar iron heated by means of a spirit lamp," a process which exhausted the patience when applied to the refractory masses in the shape of official plasters.

Plasters with an India rubber base had their origin about the year 1845, when Horace Bay and Dr. Shecut invented a combination of India rubber and the gums ordinarily used in the plaster mass; this they spread in a crude way and made the plaster porous. The process used by them was to dissolve the rubber in a solvent, such as benzin, turpentine, and bisulphide of carbon, and to this they added the gums and spread the mixture with a brush on a fabric. The process was the subject of a patent, which was sold to Dr. Thomas Allcock, and the plasters known as "Allcock's Porous Plasters" originated from this effort.

Some years later a process of mixing the rubber with gums and calendering the mass on fabric was perfected by Dr. John W. Newell, a rubber manufacturer, of New Brunswick, N. J. The process was covered by patents and secrets and was not applied to pharmaceutical plasters until many years later.

Few who now use the elegant plasters found in the market

realize what a combat with difficulties there has been to bring them to their present high standard. Probably no other branch of the pharmaceutical art has been the occasion of so much toil, anxiety, and discouragement before any measure of success was met in a pharmaceutical, commercial, or therapeutic sense. The evolution of India rubber plaster making has now reached a point where it not only requires a large amount of machinery, but a vast amount of detail in every step, which only long experience and accurate judgment can give. Prominent among the names connected with plaster making are those of Dr. Grovenor, of Boston, Mass., the late George J. Seabury, and the late Robert W. Johnson, of Johnson & Johnson, New Brunswick, N. J. It is to these men that we are indebted for the idea of making pharmaceutical plasters with a rubber base and for the great benefits which have accrued to medicine and surgery through the improvement in the art.

These manufacturers first used what is known as the benzin process. After considerable struggling they found that many of the medicaments of the Pharmacopœia were not compatible with rubber dissolved in a solvent, and the products were not fitted for therapeutic use and were worthless commercially. Benzin plasters are still made, but they rapidly decompose and many pharmacopœial drugs are useless in such a combination.

The pioneers in India rubber plaster making found that mechanical troubles were not all that were to be overcome, and it was only after a long struggle that the point was reached where the required pharmaceutical combination could be made and marketed in the shape of India rubber plasters, and it was not until a few years ago that it was recognized that a plaster was valueless to medicine and pharmacy if only the mechanical perfection was considered, without regard to the therapeutic efficiency and certain other requirements. It was, therefore, determined that mechanically the plasters should be made perfect and above all that the medication should be absorbed by the integument and thus make the plaster not only a mechanical application, but a therapeutic agent.

These conditions have not yet been completely fulfilled. It is undoubtedly true that rubber base plasters are superior as therapeutic agents to those made with a resin or diachylon base, and the rubber base plasters have been improved in such a way as to

render action of the medicinal agents contained therein possible. From a therapeutic point of view it seems to be true that a rubber base plaster will, under some conditions, promote, and under other conditions hinder, absorption.

Attempts have been made from time to time to produce excipients which would soften the base, also to add mild detergents which would soften the epidermis and thus assist in promoting absorption. Some years ago a special line of dermal plasters was offered, where a large amount of drug was held in perfect contact with the diseased skin, forming a vapor chamber.

I do not think that the plaster makers' art has anywhere nearly reached its limit, we are still looking for the ideal plaster mass. We need a compound of the peculiar nature of our present mass-elastic, adhesive at body temperature, easy of removal, but which will, in addition to the properties of the present mass, have a softening effect upon the skin. It would be desirable to have a mass which could be compounded with a more extended range of medicines. The present rubber mass will not admit of the use of many desirable combinations; for example, certain metals, such as lead, copper, iron, etc., cannot be compounded with the rubber mass. India rubber mass plasters are useless when the medicament is a free alkaloid. Oils and fats are to a limited extent only useful in the rubber combination.

The advantages of India rubber plaster mass, both for adhesive plasters and for medicated plasters, are well known. They have been summarized as follows: Purified rubber is a neutral element, and especially valuable as a vehicle for plasters on account of its great elasticity and flexibility. India rubber preserves the incorporated medicaments from evaporation and from decomposition. India rubber is highly resistant to moisture and to atmospheric influences. It has been stated by well-known therapeutists that a medicament properly combined with adhesive agents containing rubber, gives increased local action of the incorporated drug.

India rubber plasters adhere closely to the skin; they adhere at the temperature of the body without added heat or moisture. They are perfectly pliable at any temperature, and when once applied they do not slip or move, and they remain serviceable longer than any other form of plaster mass. This latter statement is undoubtedly true. Those who are familiar with the rapid decomposition which takes place in a resin and diachylon base

plaster, will at once agree as to the superior keeping qualities of an India rubber plaster. In the writer's practice he has known India rubber base plasters to keep perfectly for fifteen years.

The making of India rubber plasters is hardly within the province of a retail pharmacist. In fact, it is an art which requires the installation of large and expensive apparatus. The process has often been described. It is perhaps sufficient to state that the processes outlined in the United States Dispensatory are substantially correct.

Rubber plasters, for the most part, are made by combining India rubber, two parts, with burgundy pitch, one part, and to this is added gum, olibanum, galbanum, wax, sometimes olive oil, fillers, such as orris root, to complete the mass. Masses of this character vary with each individual plaster or medication, an acceptable plaster being one which shall contain at least  $33 \frac{1}{3}$  per cent. rubber.

The rubber to be used in a plaster mass is crushed, washed in alkaline water to remove the natural acids, resins, dirt, etc., it is then ground until plastic, and combined with the gums and with the medicaments. The process of crushing, grinding, and mixing is conducted by means of large iron rollers, an essential feature of the process being the use of great pressure instead of the heat employed in the ordinary process of plaster making. The plasters are finally spread upon the cloth by means of heavy iron rollers, on an apparatus known as a calender. In the writer's laboratory this calender weighs 20,000 pounds, and here the spreading is accomplished by pressure and the avoidance of heat. The finished plaster after being spread is allowed to stand or set. It is then wound upon cylinders, cut into shapes and lengths, such as rolls of varying widths and lengths, or into the ordinary size,  $5 \times 7 \frac{1}{2}$  inches, the latter usually being perforated.

In the eighth revision of the Pharmacopœia a notable change was made in the formula for plasters by introducing a new mass under the title of "Emplastrum Adhæsivum" as follows:

EMPLASTRUM ADHÆSIVUM  
Adhesive Plaster

Rubber, cut in small pieces, twenty grammes.....	20 Gm.
Petrolatum, twenty grammes .....	20 Gm.
Lead plaster, nine hundred and sixty grammes.....	960 Gm.

To make one thousand grammes .....1000 Gm.



"Melt the rubber at a temperature not exceeding 150° C. (302° F.); add the petrolatum, and continue the heat until the rubber is dissolved. Add the lead plaster to the hot mixture; continue the heat until it becomes liquid, then strain, allow it to cool, and stir until it stiffens."

The mass here given was intended as an adhesive plaster, and also to be used as a base or vehicle for belladonna plasters, capicum plasters, and opium plasters. In the previous edition of the Pharmacopœia the base or mass in most instances had been a combination of resin and lead plaster masses. Masses of this character had been official in several of the previous revisions. It has been stated that the present mass was introduced for the reason that non-rubber plasters had been entirely superseded by plasters with a rubber base, and that while non-rubber plasters had been retained in the U. S. Pharmacopœia in the several revisions, they had become entirely obsolete, and it was the intent of this innovation to improve the plaster mass so as to make them respond to the requirements for an India rubber base plaster.

It has been stated that the formula of the Pharmacopœia would enable the pharmacist to prepare and spread rubber base plasters, and that as a final result the lost art of plaster spreading would be restored to pharmacy. Experience, however, has shown that plaster spreading in pharmacy is no more popular to-day than when the present edition of the Pharmacopœia was issued, and, indeed, the present mass of the Pharmacopœia is not as popular as were the plaster masses of the previous Pharmacopœia.

The reasons for this condition are plain. The mass of the Pharmacopœia contains 2 per cent. of rubber, 2 per cent. of petrolatum, and 96 per cent. of lead plaster. This falls far short of the requirements for an India rubber plaster mass. The India rubber adhesive plasters, such as are sold in the market at the present time, contain from 20 to 50 per cent. of India rubber; the medicated India rubber plasters contain from 20 to 40 per cent., and it is the use of India rubber in these proportions that gives to India rubber plasters their peculiar consistency and properties.

It is my judgment that the finished plaster mass of the Pharmacopœia contains little or no rubber, as such. In making up the mass it is required that the rubber shall be melted at a temperature of 150° C. (302° F.), it is then combined with petrolatum and lead plaster mass. India rubber is decomposed at a temperature

below the point named. India rubber is decomposed in the presence of almost any fat, and especially in the presence of petrolatum. India rubber is rapidly decomposed under the influence of heat, it is also decomposed in the presence of many metals, and it is especially acted upon by lead. Such a combination, in the course of time, has a tendency to harden and become entirely useless as a plaster mass, and it would be better from a therapeutic and mechanical point of view if the India rubber had been omitted from the formula altogether. It is my judgment that the finished mass is not at all comparable with the diachylon mass, or the resin mass of the former Pharmacopœias.

The mass of the present Pharmacopœia, when freshly made and warm enough to spread, is a soft, sticky, unusable stuff. It is not to be wondered at that the profession have never adopted plasters made by the present Pharmacopœial methods, and that they rely as heretofore upon India rubber plasters, or the resin and lead plaster masses.

In addition to the plasters which I have named, the U. S. Pharmacopœia VIII has a formula for mercurial plaster made up with metallic mercury, the oleate of mercury, all combined with a lead plaster base. In this formula hydrous wool fat is used for the purpose of extinguishing the mercury. There are also given formulas for lead plaster and soap plaster, the latter being a combination of soap and a lead plaster base.

Diachylon plaster has a fairly good sale, but inquiry reveals the fact that the most of it is purchased ready spread under the types known as Maw's and De La Cour's. These types correspond quite nearly to the diachylon plaster of the U. S. Pharmacopœia of 1890, or the British Pharmacopœia of 1898, with the addition of a certain amount of resin.

The process given for capsicum plaster in the last revision directs that the oleoresin of capsicum be smeared over adhesive plaster. This process affords a convenient way of obtaining the effects of capsicum, and is capable of considerable amplification, and points out a method whereby medicated plasters may be prepared extemporaneously. Medicaments usable as external applications may be brushed over the surface of adhesive plaster and an infinite variety of medicated plasters prepared at short notice.

In this connection I call attention to the fact that, in addition

to the ordinary uses for India rubber adhesive plaster in operative surgery, there is a rapidly increasing field opening for its use as a therapeutic application. A glance at the medical journals of the last few years reveals many methods whereby such an application is being made. For example, I note the application of adhesive plaster in various forms for corns, bunions, swellings, inflammations, glandular enlargements, œdema, mammitis, mammary abscess, inflamed joints, gout, rheumatism, effusions, varicose veins, ulcers, pleurisy, pleuropneumonia, hiccough, bronchitis, neuralgia, lumbago, prolapsed stomach, floating kidney, excessive sweating, frost bites, tuberculosis, adenoids, boils, carbuncles. These varied and constantly increasing uses suggest that possibly in many instances medicated plasters would be indicated, thus giving the action of certain medicaments in addition to the mechanical and physical action of the plaster. One writer has suggested the covering of the part, to which adhesive plaster is applied, with certain medicinal agents and then applying the plaster. The process which I have outlined of brushing or spreading the medication over adhesive plaster would seem to be the more acceptable.

In the Pharmacopœia of 1880, belladonna plaster was prepared with the alcoholic extract of the root. This was also the case with the British Pharmacopœia of 1898. The revisions of the U. S. Pharmacopœia of 1890 and 1900, however, substituted the extract of the leaf for that of the root. No good reason seems to have been advanced for this change, and many reasons could be urged in favor of the extract of the root.

A plaster of the strength of that of the present Pharmacopœia, made with the extract of the leaf, is so filled with the peculiar waxy, resinous constituents of the leaf, and so colored with chlorophyll as to be highly objectionable. The belladonna plasters of the market are made almost entirely from the root. A plaster thus made either by using the base of the Pharmacopœia or an India rubber base, is easier to spread, more adhesive, and altogether more desirable than that made from the leaf, and in my judgment in the forthcoming revision the extract of the root should be restored to its former place in the making up of a plaster.

Neither the Pharmacopœia of 1880 nor that of 1890 established a definite alkaloidal strength for belladonna plaster. As a consequence belladonna plasters could be found in the market varying all the way from the slightest trace of alkaloid up to and above

the amount now prescribed as the standard. The result was not only confusing, but in certain instances serious consequences arose therefrom. The eighth revision of the Pharmacopœia established the standard of 0.38 to 0.42 per cent. alkaloid. The British Pharmacopœia of 1880 had no definite alkaloidal standard for this plaster, but the British Pharmacopœia of 1898 prescribed that belladonna plaster should contain 0.5 per cent. of the alkaloid of belladonna root.

It is the opinion of many authorities that both of these standards are high. Numerous instances have arisen whereby the constitutional effects of belladonna have been produced by the application of belladonna plasters. The Pharmaceutical Society of Great Britain has promulgated a formula for a milder belladonna plaster standardized to 0.25 per cent. alkaloid, giving as a reason therefor that a plaster of such a strength was less likely to produce poisonous symptoms than that made in accordance with the British Pharmacopœia.

My suggestion would be that the standard strength for belladonna plasters should be 0.3 per cent. of the alkaloids of belladonna.

In addition to the plasters of the Pharmacopœia, we find a number of kinds in the National Formulary. In the third edition of this book we have aromatic or spice plaster—a combination of cloves, cinnamon, ginger, capsicum, and camphor, with cottonseed oil and lead plaster as a base; camphorated brown plaster, which resembles the camphorated mother's plaster of the German Pharmacopœia, and is made up of red oxide of lead, olive oil, and camphor; compound tar plaster, which is composed of tar, podophyllum, and poke root combined with resin. These last two plasters are of the nature of the old time sticking salves, scarcely resembling the modern conception of a plaster.

In the addenda to the National Formulary we have ammoniac plaster, which is made up entirely of gum ammoniac; ammoniac and mercury plaster, consisting of gum ammoniac and oleate of mercury combined with a lead plaster base; arnica plaster, which is prepared with the extract of arnica root combined with resin plaster; asafetida plaster, a combination of asafetida, lead plaster, galbanum, and yellow wax; strengthening plaster, consisting of ferric hydroxide combined with olive oil, burgundy pitch, and lead plaster; burgundy pitch plaster, a combination of burgundy pitch, olive oil, and yellow wax; Canadian pitch plaster, consisting of



Canadian pitch and yellow wax; cantharidal pitch plaster, which is essentially the warming plaster of the U. S. Pharmacopœia of 1890 and is made up of cantharidal cerate combined with burgundy pitch; resin plaster, which is essentially the adhesive plaster of the U. S. Pharmacopœia of 1890, being a combination of lead plaster, resin, and yellow wax.

It should be noted that in the National Formulary there is no attempt to introduce India rubber into the compound, and that the formulas given in this work are those which have come down through the ages of pharmacy. It should also be noted that we have an adhesive plaster in the Pharmacopœia and an adhesive plaster in the National Formulary which are entirely different in their constituents, as well as in the resulting product.

In view of the fact that the National Pure Food and Drugs Law and the enactments of the various states have named the U. S. Pharmacopœia and the National Formulary as the standard for medicinal preparations, it seems imperative that the Pharmacopœia should name the standard for plasters in common use. Such being the case, and in consideration of the fact that plasters made with the official bases have but little or no sale, in my judgment, this course could be pursued with prescribing what the mass of the base or vehicle should be. In other words, latitude might be allowed in the selection of the ingredients of the plaster other than the medicament. This course would allow the plaster maker or the dispenser to supply plasters to suit the demand; it would enable the physician to know the exact amount of medication present in a given plaster mass, whatever might be the vehicle employed.

In my judgment the Pharmacopœia should also prescribe processes by which plasters, especially those containing alkaloids, could be assayed. The law and trade customs now require that there shall be some authority to which all things may be referred, and the Pharmacopœia alone is such an authority, and whatever else we find in such a work we should find the standard for medicinal preparations and the methods by which a given substance may be compared with the standard.

Rather than to eliminate from the Pharmacopœia a single plaster or a single preparation for which there is a reasonable demand, I would urge the addition of a still greater number. I have also suggested to the revisers of the Pharmacopœia that the formulas for plasters should be revised: That the mass or base introduced

into the last revision under the head of "Adhesive Plaster" should be abandoned, and a mass or base more nearly resembling that of the old base of 1880 be restored: That if such a course could be made possible, the alternate use of any India rubber mass, such as now employed by manufacturers, be allowed: That assay processes be prescribed for all plasters containing alkaloids or definite medicinal medicaments.

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## SCAMMONY AND RESIN SCAMMONY.\*

BY H. ENGELHARDT and M. R. SCHMIDT.

Considerable work has recently been done on the chemical and physical properties of the several substances generally classed as scammony resins. Guigues,<sup>1</sup> Cowie,<sup>2</sup> and Taylor<sup>3</sup> have made important contributions to our knowledge of these bodies, but it appears that the end is not yet reached.

The whole subject is more complicated than would appear at first sight, and great confusion exists, especially in the minds of dealers, as to what is covered by the terms scammony and resin scammony.

The U.S.P. recognizes as official two substances: scammony, which is the exudate obtained by incising the living root of *Convolvulus scammonia*, and resin scammony, which is prepared by extracting scammony with alcohol, precipitating the resin with water, and drying at a gentle heat.

The French Codex recognizes the same substances.

The British Pharmacopœia, on the other hand, describes virgin scammony, resin scammony, and scammony root; the virgin scammony is used without further purification, and the resin scammony is made by extracting scammony root with alcohol. Consequently resin scammony of the British Pharmacopœia is not necessarily identical with resin scammony of the U.S.P. or the French Codex.

Of late years there has appeared on the market another substance, the so-called Mexican scammony, prepared by extracting

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\* Read at the meeting of the A. Ph. A. at Richmond, Va., May, 1910.

<sup>1</sup> *Journ. de Ph. et de Ch.* (6) 11; 529 (1900); *ibid.* (6) 22; 24 (1905); *ibid.* (6) 24; 404, 440, 498 (1905); *Bull. Soc. Chim.*, 872 (1908).

<sup>2</sup> *Trans. Brit. Pharm. Conf.*, 1908; 457, 462; *Pharm. Journ.*, Dec. 25, 1909.

<sup>3</sup> *AM. JOURN. PHARM.*, vol. 81, 105 (1909).

the root of *Ipomæa orizabensis*. This substance is not yet official in any of the pharmacopœias.

The subject is further complicated by the difficulty of procuring authentic samples. The dealers frequently confuse names, and, judging by our analytical results, substitution very often takes place. As an example, one lot of root shipped as genuine Mexican scammony was labelled "*Convolvulus Scammonia*, Mexican," which is of course contradictory.

The work of Guigues dealt principally with the solubility of scammony resin in ether, and with the optical rotation. He found that some scammony resins were partly insoluble in ether, while the resin from *Ipomæa orizabensis* is completely soluble in ether and can be used to adulterate true scammony, a statement, which, as will be shown later, is incorrect. He also called attention to the necessity of using ether of a definite degree of hydration and alcohol percentage when determining the solubilities.

As regards the optical rotation for resin extracted from the gum resin (scammony), Guigues found a maximum specific rotation of  $-24.5^{\circ}$ . For resin extracted from the root, the rotation varied from  $-18.5^{\circ}$  to  $-23.5^{\circ}$ .

The work of Cowie showed that the saponification value is a simple and accurate means of distinguishing true scammony resin from Mexican resin. Cowie also studied the solubility in ether.

Taylor has also made a rather extended study of the acid and saponification numbers, ether solubilities, and iodine numbers of various scammony resins. According to his statement, however, all these resins were prepared by extracting the roots with alcohol, and hence none of them can be regarded as U.S.P. products.

Cowie does not give any details as to the history of most of his resins, but it appears that most of them were commercial samples, or purified resins obtained from commercial articles. If his resins were prepared by purifying virgin scammony, they would come under the class of the U.S.P. resin scammony, but would not be official in the British Pharmacopœia, and vice versa, if they were made by extracting the drug, they would be official in the British Pharmacopœia and not in the U.S.P. This instance shows the difficulty of arriving at definite conclusions in these matters.

The chief results of Taylor's and Cowie's work have been to show that the saponification values for resins from *Convolvulus scammonia* range around the number 238, while the saponification values

of the resins obtained from the Mexican root are generally less than 190. Taylor, using U.S.P. ether, found that both the Mexican and the true scammony resins, with the exception of one sample, were at least 99 per cent. soluble in ether. This does not agree with the statement of Cowie, who finds that true scammony resin is soluble from 96.4 per cent. to 100 per cent. in ether of sp. gr. .720, while three samples of the Mexican resins were dissolved only to the extent of 68.6 per cent. to 72 per cent. Cowie has directed attention to the varying solubility which will be found if the ether used in the different determinations is not perfectly uniform in quality. This fact may account for the discrepancies between Taylor's and Cowie's results. A more detailed discussion of this point will be taken up later.

The resins examined in this work were all purified according to the U.S.P. method, *i.e.*, extracting with boiling alcohol, with precipitation of the concentrated extract by water and subsequent drying. In order to insure more perfect drying, without the danger of overheating, all our resins were dried in the following manner. After thorough washing, the resinous mass was freed from inclosed water by stirring and draining. It was then dissolved in alcohol, filtered, and the alcoholic solution evaporated to a thick syrup, which was then poured on thin sheets of glass and dried at a temperature slightly below 100°. The results show that the moisture content of resins dried in this way is no less than is found in those which have been dried by other methods. The alcohol was certainly eliminated, but it appears that a temperature above 100° is necessary to remove the water entirely. The U.S.P. direction to dry at "a gentle heat" therefore seems inadequate.<sup>1</sup>

The moisture determination was made by heating the powdered resin on a watch glass for one hour at 110° to 115°. Our results are practically identical with those of Cowie and Taylor, and the same is true of the percentage of ash.

The determination of the acid number often offers considerable difficulty, on account of the dark color which the solution assumes almost immediately after the addition of any alkali. Recourse was finally had to the method of Marx.<sup>2</sup> Two grammes of the powdered resin are dissolved in a large flat-bottomed porcelain dish in

<sup>1</sup> The French Codex directs 45° C.

<sup>2</sup> *Chem. Ztg.*, No. 16, 1910.



about 100 c.c. of neutral alcohol, and the titration made with one-half normal alcoholic potash and phenolphthalein. The solution of the resin is thus brought against a white background, in a thin layer, which facilitates the determination of the end point. Even with this aid, however, the determination is not always satisfactory, and little confidence can be placed in the accuracy of the results. An attempt to use  $\frac{N}{4}$  barium hydrate solution was unsuccessful, since the color developed, if anything, was darker than that caused by the potassium hydroxide.

The saponification values were determined in the usual way, using  $\frac{N}{2}$  caustic potash.

Ether solubilities were determined in both commercial and anhydrous ether. The commercial ether had a sp. gr. of .7128 at 25°, while the anhydrous ether had a sp. gr. of .7106. It will be noted, as Cowie has already pointed out, that the ether solubility varies with the nature of the ether used.

A rather extended study of the iodine numbers was made. The method by Hübl was applied at first, but it was found to be impossible to obtain concordant results by it. The iodine numbers varied in some cases 100 per cent. when the different tests were allowed to stand for different lengths of time. Moreover, no definite end-point could be found when titrating the excess of iodine with sodium thiosulphate and starch indicator. The solution continually became blue within ten seconds after being decolorized, and this often continued during the addition of 3 to 5 c.c. of thiosulphate solution. This method was finally given up and the determinations were made according to the method of Wijs.<sup>1</sup> This method has proven itself to be so satisfactory that we can recommend it most highly, at least when working with these resins. The solution is prepared as follows: 9 Gms. of powdered iodine are dissolved by the aid of heat in 500 c.c. of glacial acetic acid. Chlorine gas, washed through water, and dried by sulphuric acid, is then passed into the solution, using a capillary tube to insure more complete absorption. Thus the iodine is converted into iodine monochloride. The completion of the reaction is shown by the sudden disappearance of the dark-brown color of the solution, and this end-point is very

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<sup>1</sup> *Berichte*, 31; 750 (1898); *Chem. Rev. Fett-u. Harz-Ind.* 6; 5; see also the excellent article by Harvey, *Journ. Soc. Chem. Ind.* 21; No. 23, 1437 (1902).

easily seen. About one-tenth of a gramme more of iodine is added, until the dark color of the solution is partly restored. This is done to prevent the solution containing an excess of chlorine. To make a determination, 1 Gm. of the powdered resin is put into a glass-stoppered 200 c.c. bottle, 10 c.c. of redistilled carbon tetrachloride free from carbon disulphide or oxidizable substances are added, and 25 c.c. of the iodine monochloride solution. After standing for one hour in the dark, 20 c.c. of 10 per cent. potassium iodide solution are added and 50 c.c. of distilled water, and the excess of iodine titrated back in the usual way. The end-point is very sharp and there is very little tendency for the blue color to reappear. One sample which was allowed to stand for 15 hours required only 0.3 c.c. more of tenth-normal thiosulphate solution to titrate the iodine which had separated.

The iodine numbers obtained by Wijs's method were in every case higher than those obtained by Hübl's method, even when the latter solutions were allowed to stand for twenty-four hours. Blank determinations are unnecessary with Wijs's method. The equivalent of 25 c.c. of the solution in terms of sodium thiosulphate solution is determined once for all, and the solution is so stable that subsequent blanks are not necessary. The solution of iodine monochloride can be prepared in one-half hour, and for most oils and fats from fifteen to forty minutes is sufficient time for complete absorption of the iodine. The behavior of the scammony resins toward Hübl's solution led us to consider one hour as a sufficient time, but it may be said that no difference was found when the absorption was continued for one-half hour longer.

The optical rotations were determined with the decolorized resin in the following way: about 4 Gm. of the resin were dissolved in about 50 c.c. of alcohol, water added almost to turbidity, and the solution boiled for one hour with about 2 Gm. of animal charcoal, using a reflux condenser. After settling, the solution is cooled, and the liquid poured through a filter. A second treatment with animal charcoal generally suffices to give a solution which is almost colorless. After filtering, 10 c.c. of this solution are removed by a pipette to a small tared beaker, evaporated to dryness, dried at 110° and weighed. Another portion of the solution is polarized in a 10 cm. tube.

In order to confirm the results of previous observers, and to orient ourselves regarding virgin scammony and Mexican scammony

resin, the specimens marked I, II, III, and IV in the tables were prepared. Number I came to us labelled "Virgin Scammony, elect." In its physical appearance it agreed with the descriptions in the text-books. It was of a greenish-brown color, very brittle, and its lustre would have been classed as subresinous in mineralogy, since the fracture was almost without gloss. It was also of a granular or porous texture. No gross impurities were visible, such as pebbles, woody matter, etc. In our opinion, this sample was actually the exudate from *Convolvulus scammonia*, which had possibly been freed from coarse impurities by fusing and straining.

A purified resin obtained by extracting a portion of I with alcohol, precipitating with water, etc., constitutes specimen II. Number II presented an appearance entirely different from I. It was of a yellowish-brown color, semitransparent, not very odorous, and its lustre was markedly resinous.

III was prepared by percolating a lot of root which had been labelled "True Scammony Root." Microscopic examinations bore out this statement.

IV was obtained by percolating a lot of drug identified as *Ipomœa orizabensis*.

These samples were compared with three products marketed under the names of virgin scammony and scammony resins. Specimen V was labelled "Scammony Resin Virgin." Its appearance was totally different from that of I, its lustre was perfectly resinous, its color dark brown, and instead of being porous, the pieces were perfectly homogeneous like ordinary resin. Its odor, moreover, was cheese-like. Judging from its appearance, and more especially from its physical and chemical constants, this sample was wrongly labelled. Before use it was purified in the usual way.

Specimen VI was labelled "True Scammony Resin," and in general appearance was identical with V. This sample had also been misbranded.

Sample VII was labelled "Resin Scammony." In appearance it was like V and VI, but its odor was slightly like pepper. It was examined both in the ordinary state in which it was received, and after having been purified, the purified sample constituting specimen VIII. The results show that it was also made from the Mexican root, and therefore was wrongly labelled.

The following results were obtained and are arranged in three tables. Table I includes moisture, ash, acid, saponification and ester

numbers. As stated before, the moisture content of these resins was not reduced by the method of drying adopted by us. The results agree perfectly with those found by Cowie and Taylor and no further comment is necessary, except to call attention to the high percentage of moisture in the commercial samples I and VII.

The percentage of ash is rather constant, and in all cases except I is well below the limit of 1 per cent. allowed by the U.S.P. for resin scammony. The percentage of ash found in I is also below the limit of 3 per cent. allowed by the U.S.P. for virgin scammony; this high percentage of ash confirms our belief that the resin had been only superficially purified by straining from gross impurities.

Nothing definite can be concluded from the acid numbers, as has already been stated by Taylor and Cowie. The saponification numbers, on the other hand, fall into two well-defined groups. I, II, III have saponification numbers which are considerably over 200. II, which may be taken as a representative sample of purified virgin scammony, has the value 236.6 which is in close agreement with the average of about 238 found by Taylor, Cowie, and others. The saponification value of the other five samples range within narrow limits around the number 177, which is lower than the average saponification value obtained by Taylor and Cowie.

Table II shows the solubility in various solvents. The most important results are the solubility in ether. Cowie and Guigues have, as already stated, directed attention to the necessity of using anhydrous ether in determining the solubility, and their results are fully confirmed by the present work.

Sample I, the most impure specimen of all, was soluble to the extent of 71.8 per cent. in dry ether, but to the extent of 85 per cent. in commercial ether, thus passing the requirements.

Sample II, the purified resin prepared from I, was entirely soluble both in anhydrous and commercial ether. III was soluble to the extent of 96 per cent. in commercial ether, and by stretching the words "almost completely" might have passed muster as the U.S.P. article, although it was prepared by percolating scammony root. The other five specimens vary between 80 and 90 per cent. soluble in hydrous ether, and were all nearly 90 per cent. soluble in anhydrous ether. In this connection we must call attention to the phenomenon always noticed when dissolving Mexican scammony in ether. Using U.S.P. ether, containing varying amounts of water and alcohol, a part of the resin invariably separates



as a varnish on the walls of the vessel. This does not take place with resin made from scammony or from scammony root, and this appearance can be used to detect Mexican scammony in the presence of a considerable quantity of true scammony resin. Using anhydrous ether, the insoluble portion assumes a granular form, which on standing settles to the bottom as a sticky mass.

The portion insoluble in chloroform was generally gelatinous and rather dark in color.

We have already spoken of the difficulty encountered in determining the iodine numbers by the method of Hübl. For example, sample II after being allowed to stand for four hours gave an iodine number of 5.5; after standing for fifteen hours this value had risen to 8.8; and another test which was allowed to stand for twenty-four hours showed only 8.22. Sample V with Hübl's method gave 8.38 after five hours and 10.58 after fifteen hours, while the same resin by Wijs's method gave 11.6 in one hour. The average of our iodine values is slightly greater than the average of Taylor's. As can be seen from the tables, no definite relation exists between the variety of resin and the iodine value, and this method cannot be used as a means of differentiating the resins. We wish, again, however, strongly to recommend the method of Wijs. It is convenient, rapid, and accurate, duplicate determinations agree well, the end-point is sharp, and work is considerably lessened by the fact that the solution is stable and blanks are unnecessary for each determination. The solution should be kept in a dark bottle, otherwise the acetic acid is likely to be substituted by the halogens and the solution will lose in strength.

The specific rotations also fall into two distinct groups. The values found for the resins known to be derived from *Convolvulus scammonia* are close to  $-24^{\circ}$ , while those for the Mexican resins are all over  $-31^{\circ}$ . Guigues, as mentioned before, was the first to call attention to this fact. Our value of  $-25.98^{\circ}$  for sample I is slightly higher than his maximum of  $-24.5^{\circ}$  obtained for a specimen prepared in an identical manner, and our value of  $-24.24^{\circ}$  for sample III is slightly higher than his limit of  $-23.5^{\circ}$  for resin extracted from the true root. These determinations can be made with a considerable degree of accuracy, and the optical rotations furnish a valuable means of distinguishing the true and false resins. The specific rotation of the Mexican resin approaches the specific rotation of resin jalap, but the high price of resin jalap would prevent any adulteration of Mexican resin with the former.

It is a well-known fact that virgin scammony is getting to be a scarce article, and it is almost impossible at the present time to obtain any large quantities of the authentic substance. Moreover, all the work that has been done so far goes to show that the resin prepared by extracting the root of *Convolvulus scammonia* is practically identical with resin scammony prepared according to the U.S.P. directions from virgin scammony. We would suggest, therefore, if resin scammony is to be retained in the Pharmacopœia, that the Revision Committee make the resin extracted from the root official, as has been done in the British, Belgian and Italian Pharmacopœias. On the other hand, if it can be shown by physiological experiments that the Mexican resin is identical in its action with true resin scammony, there seems to be no good reason why that cheap and abundant article should not replace the latter.

TABLE I.

Sample.	Moisture. Per Ct.	Ash. Per Ct.	Acid No.	Sap. No.	Ester No.
I.	6.16	2.70	18.5	207.2	188.7
II.	1.95	.00	10.6	236.6	226.0
III.	2.07	.21	16.3	256.2	239.9
IV.	1.45	.20	10.2	175.8	165.6
V.	2.25	.07	12.2	177.1	164.9
VI.	2.23	.20	14.0	171.6	157.6
VII.	4.29	.30	13.6	183.8	170.2
VIII.	2.03	.15	14.9	175.9	161.0

TABLE II.

Sample.	Soluble in Abs. Ether.	Sol. in U.S.P. Ether.	Sol. in Chloroform.	Sol. in Alcohol.
	Per Cent.	Per Cent.	Per Cent.	Per Cent.
I.	71.8	85	82.1	90.6
II.	100	100	100	100
III.	93.9	96.0	100	100
IV.	89.4	84.1	98.0	100
V.	90.2	85.5	98.9	100
VI.	88.3	80.9	96.1	100
VII.	89.6	82.0	96.9	100
VIII.	90.4	91.5	97.4	100

TABLE III.

Sample.	Iodine No.	Optical Rotation. Degrees.
I.	11.69	—25.98
II.	10.45	—24.97
III.	17.83	—24.24
IV.	11.60	—32.78
V.	11.48	—33.80
VI.	13.93	—34.27
VII.	12.46	—31.31
VIII.	11.65	—31.83

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 Baltimore, Md.

## A NOTE ON OIL OF GAULTHERIA.\*

BY GEORGE M. BERINGER.

Early in June of last year, I had collected near Hammonton, N. J., a quantity of the plant *Gaultheria procumbens* L. and expressed to me in the fresh condition. This was carefully garbled over to remove any admixed plants or leaves, and adhering dirt washed off. It was then distilled in a copper still with jet of live steam continuously thrown into the still, so as to prevent charring and at the same time thoroughly extract the oil. From 4070 Gm. of the plant I obtained 23.63 Gm. of oil, equivalent to a yield of 0.586 per cent. It is to be noted that the writer used the entire plant for his experiment.

About the same time, Professor Henry Kraemer had distilled in his laboratory at the Philadelphia College of Pharmacy a quantity of gaultheria, using the leaves only which were separated from the freshly collected plants. The writer was fortunate enough to secure a sample of this oil and so has now two authentic samples of oil of gaultheria to exhibit.

While it is true that the U. S. Pharmacopœia does describe oil of gaultheria as "distilled from the leaves," it is exceedingly doubtful if in actual practice this has ever been strictly followed as

\* Presented to the New Jersey Pharmaceutical Association meeting, Cape May, June 15, 1910.

the custom is to gather over ground portions of such small procumbent plants and not expend the labor necessary to strip leaves only.

These two samples of oil exhibit some distinct differences. The sample from Kraemer's distillation is almost water white and has remained so for a year. It has a much lighter, more ethereal odor while that from my own experiment has gradually darkened and assumed a pale amber tint and has a much heavier odor: both color and odor more closely resembling that of the distilled oil commonly appearing in commerce.

The specific gravity and optical rotation of these oils is as follows:

	Sp. Gr.	Optical Rotation.
Kraemer's .....	1.1785	—0.26°
Beringer's .....	1.177	—1.335°

While there is scarcely any difference in the specific gravity of the samples there is marked difference in the lævo-rotatory power. In this connection the U. S. Pharmacopœia states that oil of gaultheria is lævo-gyrate up to  $-1^{\circ}$  in a 100 mm. tube, at  $25^{\circ}$  C. If the oil from the entire plant is to be officially recognized then the writer's experiment demonstrates that this limitation must be somewhat extended.

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## PROGRESS IN PHARMACY.

By M. I. WILBERT, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

The meetings of state and national associations, both medical as well as pharmaceutical, that have been held during the past three months are destined to have a very far-reaching influence on the future development of pharmacy.

The proceedings of the several state pharmaceutical associations have been reported at length in the several trade journals and from the published reports it would appear that the meetings were unusually well attended and that considerable time was devoted to the discussion of scientific papers and subjects.

As usual the proceedings of the Missouri Pharmaceutical Asso-



ciation are the first to be published, and Secretary Whelpley is to be congratulated, not alone for his promptness, but also for presenting so complete a report in the short time intervening. The book contains 177 pages and is liberally illustrated. The meeting of the Missouri Association was held in Maryville, June 14-17, 1910, and was quite an innovation in that the members occupied a tent city.

THE MEETING OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION will no doubt serve to arouse interest, not alone in Pennsylvania, but throughout the several states of the Union. A comprehensive legislative program was outlined and put in effect the resulting laws will establish for American pharmacy a new and decidedly higher ideal than has been evidenced heretofore.

In the matter of scientific papers the Pennsylvania Association again leads all of its competitors and the association honored itself by electing to the presidency Prof. Chas. H. LaWall who, for a number of years, has been directly responsible for the unusually large number of papers read at the meetings of the Pennsylvania Pharmaceutical Association.

THE AMERICAN CHEMICAL SOCIETY.—The summer meeting of this society was held in the city of San Francisco, July 12-15, 1910, and while not so largely attended as some of the previous meetings in the eastern section of the United States, appears to have been thoroughly satisfactory to the members who had an opportunity to attend.

AMERICAN MEDICAL ASSOCIATION.—The sixty-first annual meeting of this association was held in the city of St. Louis, June 6-10, 1910. From published reports it would appear that from a scientific or an organization point of view the meeting was a complete success.

The attendance was a little over four thousand, a number exceeded only by the meeting in Chicago, in 1908, and Boston, in 1906. Every section is reported as having held profitable sessions and the attendance at the section meetings is said to have been unusually good.

THE SESSIONS OF THE SECTION ON PHARMACOLOGY AND THERAPEUTICS were unusually interesting to pharmacists and many of the local men took advantage of the opportunity to attend and take part in the discussions.

The pharmacists of St. Louis also made a practical contribution to U.S.P. and N.F. propaganda work by exhibiting a number of

official preparations. This exhibit, and a somewhat similar exhibition from the chemical laboratory of the American Medical Association, elicited considerable attention and both were favorably commented on by the physicians who saw them.

BRITISH PHARMACEUTICAL CONFERENCE.—The forty-seventh annual meeting of the British Pharmaceutical Conference was held in the town of Cambridge during the week of July 25, 1910. The meeting has been designated as one of the best of recent years and from the published reports it would appear that it brings with it very marked changes in the association work of British pharmacists. The presidential address by Mr. Francis Ransom is a contribution of unusual merit and well worthy of careful study by American pharmacists.

The papers, according to the established custom, are reported at length in the pharmaceutical journals and while not numerous they indicate careful study and are fully representative of the scientific attainments of British pharmacists.

The paper on Liquid Extract of Ergot, by J. H. Franklin, with results of physiological tests made by G. S. Haynes, is a particularly timely one and indicative of the tremendous field for research and study that is available to pharmacists at the present time.

Several papers were devoted to the bacteriological testing of disinfectants, the object being to evolve, if possible, a method for the standardization of disinfectants. The president, in his address, points out that the difficulties met with in the investigation appear to be as great, and even greater, than those encountered in the standardization of drugs. Neither the chemical nor the bacteriological processes which hitherto have been devised seem to be applicable in all cases, although for specific purposes comparisons of efficiency may be deduced.

The social features of the meeting were, as usual, quite numerous, and the week's gatherings are generally considered to have been a complete success. The next annual meeting will be at Portsmouth and the president elected to preside at that meeting is W. F. Wells, of Dublin.

FEDERATION OF LOCAL PHARMACEUTICAL ASSOCIATIONS OF GREAT BRITAIN.—A news note points out that at the meeting of this association, held in Cambridge, on Tuesday, July 26, it was resolved to recommend that the British Pharmaceutical Conference

divide its proceedings into scientific and practical sections, the latter, including some of the matters which the conference has been in the habit of dealing with, would suffice to include the work now being done by the Federation of Local Pharmaceutical Associations of Great Britain, and the latter organization, which was founded to represent the trade interests of British chemists and druggists, is to be discontinued (*Chem. and Drug.*, London, July 30, 1910, p. 154).

BRITISH MEDICAL ASSOCIATION.—The annual meeting of the British Medical Association was held in London, beginning on July 22. One of the more interesting discussions was on the question of censorship of advertisements offered for insertion in the *British Medical Journal*. It was finally decided that this question should be carefully considered by the Central Council and that a report be prepared and submitted to the next representative meeting.

The exhibition, which is described at some length in the *Chemist and Druggist* (June 30, 1910, pp. 155-158), was particularly interesting from an American point of view, in that a very large number of preparations that have been eliminated from similar exhibitions in this country were shown.

SOCIÉTÉ DE PHARMACIE D'ANVERS has recently celebrated its seventy-fifth anniversary and the journal of the society, for June 15, 1910, is devoted to an account of the several features of the celebration and incidentally gives a review of the history and achievements of the society since its organization on May 29, 1835. The report is liberally illustrated with portraits of present and former officials and is supplemented by an appendix containing messages of greeting and felicitation from other pharmaceutical associations.

THE CENTENARY OF THE "JOURNAL DE PHARMACIE ET DE CHÉMIE, PARIS."—A comprehensive history of this journal from 1809 to 1909 has been published separately, making a volume of 102 pages, liberally illustrated.

The biographical sketches and portraits of past editors include such well known personages as: Parmentier, Boullay, Pelletier, Bouillon-Lagrange, Soubeiran, Planchon, and Riche, names well known wherever the science and art of pharmacy or chemistry are known or practised.

INTERNATIONAL CONGRESS OF PHARMACY.—The *Chemist and Druggist* (May 21, 1910, v. 76, pp. 91, 92) presents a report of

interviews with M. Derneville and M. Schamelhout, regarding the International Congress of Pharmacy to be held in the City of Brussels, September 1 to 4. The meetings are to be held in the Palais des Académies, one of the finest buildings of its kind in Brussels, and the proceedings will partake of a scientific as well as of a professional character. One of the more important questions that will be discussed will be the introduction of international methods of analysis and the use of uniform reagents. Trade interests will also be discussed at length, particularly the sale of specialties in the different countries and the formation of an international federation of pharmacists' associations.

THE REVISION OF THE U.S.P.—Never before has the Pharmacopœia of the United States attracted the attention of the more progressive members of the medical profession to the extent that is now evident, and it would appear to be desirable that members of the U.S.P. Committee of Revision and pharmacists generally acquire more than a superficial knowledge of the interest that is being evidenced and the thoughts that are being voiced. Many of the more progressive medical men appear to agree with Dr. Abraham Flexner who, in the Report on Medical Education in the United States and Canada (Carnegie Foundation for the Advancement of Teaching, Bulletin No. 4, p. 63), characterizes the pharmacopœia as "the traditional encyclopedic expression of the credulity of empiricism in medicine."

PHARMACOPŒIA REVISION.—W. A. Bastedo is quoted (*J. Am. M. Ass.*, 1910, v. 55, p. 166) as pointing out that while a large comprehensive pharmacopœia is not of necessity a disadvantage and, by allowing for a diversity of opinion, may be an advantage, medical teaching must be in advance of the profession and the selection of drugs for this purpose should be based on reliable pharmacologic and clinical data, regardless of the extent of their use.

THERAPEUTICS AS IT APPEARS FROM THE PRESCRIPTION FILE.—Dr. Julius Noer asserts that an examination of many thousands of prescriptions from the files in drug stores shows prescriptions by physicians of an inordinate mass of pseudotherapeutic agents. He believes that talismanic therapeutics did not die with Paracelsus, nor has the mother church in Boston a monopoly as a promoter of pseudoscience; and that the excellent work of the Council on Pharmacy and Chemistry of the American Medical Association is



not without cause and justification (*J. Am. M. Ass.*, 1910, v. 55, p. 343).

PHARMACOPŒIAL REVISION.—Dr. A. S. Loevenhart, in discussing the above, points out that the situation is not encouraging. The whole drug business is in a bad state in many ways. With some striking exceptions, the vast majority of drug houses are interested purely and simply in the making of money and are unconcerned with the question of public health. Moreover, our expectations with regard to the pharmacopœial convention have been absolutely disappointed. The convention was dominated by poor medical schools and the pharmaceutical associations in the interests of the drug trade. The convention refused to pass a resolution excluding from the Pharmacopœia drugs which are known to possess no therapeutic effect. It is impossible to use the Pharmacopœia with our students.

MEDICAL EDUCATION.—The Carnegie Foundation report on medical education has been widely commented on in medical and lay journals. While this report contains many statements of detail which may be criticised, the general trend of the report has been generally commended, particularly in lay journals which, like the *New York Globe*, argue: "If the doors of the state university, rich in educational opportunities, qualified to turn out real doctors, lawyers, engineers, and the like are open to all, why should the manufacture of feebly qualified professional men by others be tolerated at all."

NATIONAL FORMULARY AND THE AMERICAN MEDICAL ASSOCIATION.—Considerable space has been devoted, in recent issues of pharmaceutical and drug journals, to the discussion of the attitude taken by the American Medical Association Committee on National Formulary and the refusal to co-operate with the Committee on National Formulary in the revision of that book. Much of the published discussion is designed to confuse rather than correct existing opinions regarding the aims and the objects involved.

To be entirely clear in the matter it should be remembered that the American Medical Association through its Council on Pharmacy and Chemistry has adopted certain standards to which materia medica products are expected to comply, and it would be manifestly unfair for this association to require compliance with its standards by the preparations enumerated in *New and*

Non-official Remedies and endorse remedies contained in the National Formulary which obviously do not comply with either the letter or the spirit of the rules under which the Council is working.

The American Pharmaceutical Association, on the other hand, through its Committee on the National Formulary, has undertaken to supply a legitimate demand for authoritative and pharmaceutically reliable formulas for preparations that may or may not have therapeutic value.

The primary and, in a way, the sole object of these formulas is to secure uniformity so that a physician who chooses to use a National Formulary preparation, and writes for it as such, is assured of securing, from reliable pharmacists, preparations that are identical in strength and composition no matter where or by whom they are made.

It will readily be seen that while the objects in view in both instances are commendable they do not necessarily have much in common.

The American Medical Association, through its Council on Pharmacy and Chemistry, is endeavoring to educate physicians to the future use of acceptedly reliable medicaments, while the American Pharmaceutical Association, through its Committee on National Formulary, is attempting to supply pharmaceutically correct formulas for preparations that are, by many of the leading medical practitioners, no longer accepted as being in harmony with modern theories or practice.

As further illustrating the interest that is being manifested in rational therapy it would be desirable to call attention to a number of additional articles that have been published in medical journals. This would, however, be space consuming and for the present it may suffice to call attention to the following:

PHARMACOLOGIC FETISHISM.—Under this heading Wilfred M. Barton discusses a dozen pharmacologic questions which he designates as delusions, basing his arguments on what appears to him firm ground.

Among others, he points out the futility of using lead and opium wash in sprains, giving sparteine as a cardiac tonic and substitute for digitalis, using calomel as a cholagogue, ergot as an internal hemostatic, and sweet spirits of nitre as a diuretic or diaphoretic (*J. Am. M. Ass.*, 1910, v. 55, pp. 284-287).

C. N. Branin, in commenting on the paper by Dr. Barton, points out that every drug mentioned by the latter has been largely used by physicians with real or fancied results. He suggests that there should be no tearing down without building up and it would be well, therefore, if iconoclasts would, at the same time that they are criticising old time remedies, suggest effective substitutes (*J. Am. M. Ass.*, 1910, v. 55, p. 520).

PH. GERM. V. AND POST-GRADUATE INSTRUCTION.—A news item points out that the tests in the forthcoming new edition of the German Pharmacopœia are so novel that the Prussian Government has instituted courses for instructing the inspectors of pharmacies in the new analytical methods.

It is also proposed to institute special post-graduate courses at various universities for the benefit of owners as well as of pharmaceutical assistants. It is pointed out that the rapid strides made during the past year in analytical chemistry render it practically necessary for the pharmacist to receive proper tuition in this respect to enable him to apply the knowledge thus acquired to the best advantage in his own interests (*Chem. and Drug.*, London, July 30, 1910, p. 137).

NOMENCLATURE.—G. Grossmann, in discussing the nomenclature of the German Pharmacopœia, points out that despite the fact that this book has been repeatedly revised it still contains a very large number of incomplete and misleading names. He asserts that the book should above all be practical and designed to facilitate the everyday work of the apothecary and, above all, it should be in harmony with the usages of the time for which it is intended. Many of the points that he calls attention to are equally applicable to our own U.S.P. (*Ber. d. Deut. Pharm. Gesellsch.* Berlin, 1910, v. 20, pp. 266-277).

SYNTHETIC REMEDIES AS OFFICIAL SUBSTANCES is the heading for a timely editorial in the *Pharmaceutical Journal* (London, 1910, v. 30, p. 753). In the pharmacopœias of all countries the nomenclature of synthetic remedies has proven to be a stumbling block for one reason or another. In most cases the systematic names are out of the question while the name that has been given them by the manufacturer, even in the countries where they can be used, are so well known to the laity that their use is a doubtful advantage. In addition to antipyrin, phenacetine, salol, and sulphonal, which have been included in all of the newer pharmacopœias, the

following have been found to occur most frequently: Airol, 2; aristol, 5; aspirin, 8; benzonaphthol, 4; betol, 2; creosotal, 4; dermatol, 14; dionin, 4; diuretin, 13; doutal, 14;  $\beta$ -eucaine, 4; euquinine, 3; heroin, 6; iodol, 4; lactophenin, 3; novocaine, 2; protargol, 6; pyramidon, 3; salipyrin, 11; salophen, 4; stovaine, 2; tannalbin, 6; tannigen, 4; tannoform, 3; trional, 13; urotropin, 7; veronal, 4; xeroform, 3. These popular or trade names are, however, but seldom included as the official title.

BRITISH PHARMACOPŒIA.—The British Pharmacopœia Committee of Reference in Pharmacy has presented a second report to the General Medical Council which is summarized in the *Chemist and Druggist*, for July 2, 1910, p. 52, and embodies the results of the work accomplished in connection with the revision of the British Pharmacopœia from November 18, 1908, to December 16, 1909. The report has been published complete by Messrs. Spottiswoode & Co., Ltd., 5 New Street Square, London, and may be obtained from them post-free for 1s. 1d.

SAFEGUARDING THE PUBLIC HEALTH.—So much has been said recently in connection with the possible extension of public health work that many druggists appear to be decidedly confused regarding the desirability of having work of this kind done under the auspices of the National Government. Much of this confusion is, no doubt, due to the positive misstatements that have appeared in some of the more widely circulated trade journals and it may be reassuring to at least some to learn that the so-called medical trust is not responsible for the origin of all public health legislation.

An editorial (*American Medicine*, 1910, v. 16, pp. 339-342), in discussing the general subject, points out that: "Opposition to a national department of health from any one who does not have some selfish interest liable to be restricted or regulated by the proposed plans is quite incomprehensible.

"The fallacious argument promulgated by the 'National League for Medical Freedom' against the proposed national department of health is not apt to deceive for long any but those who wish to be deceived.

"The people will soon realize the truth, that the forces behind the 'League for Medical Freedom' are not as lily white and free from ulterior motives as those exploiting it would like to convey. Unquestionably many have been attracted to this organization in good faith and with no other object than to further the principle



of medical freedom. When such people realize that the great bulk of the regular medical profession are heart and soul with the broadest possible freedom of medical thought, teaching, and practice, and awaken to the unselfish, self-sacrificing work of the men who are bending every energy to what seems to them the *summum bonum* of present day living—the prevention of disease, it is entirely probable that any reason for the ‘League for Medical Freedom’ will cease to exist.”

The rational discussion of matters relating to the safeguarding of the public health and the prevention of diseases has been altogether too much neglected by pharmacists and it is gratifying, therefore, to learn that Prof. Joseph P. Remington discussed “The rôle of pharmacy in preventive medicine,” at one of the sessions of the Section on Preventive Medicine and Public Health of the American Medical Association (*J. Am. M. Ass.*, 1910, v. 55, p. 557).

Prof. Remington very properly asserts that: “The words preventive medicine have to a commercial druggist, a significance which he has yet failed to grasp. . . .”

It is unfortunate, however, that much of the discussion following is from a point of view that is practically negligible at the present time. It would be difficult indeed to demonstrate that disease can be communicated by means of the prescription container, even granting that the average druggist took absolutely no precautionary measures in the way of cleansing or destroying such containers.

While it may be true that some few retail druggists are careless and not too cleanly, the fault for this shortcoming is to be placed primarily at the door of the pharmaceutical schools which have as yet failed to give adequate instruction in the value of cleanliness and hygiene in general.

THE INTERNATIONAL ENCYCLOPÆDIA OF ETHICAL NON-OFFICIAL PHARMACEUTICALS.—An editorial in the *Journal of the American Medical Association* (Aug. 6, 1910, p. 519) calls attention to an evident attempt to develop the commercial possibilities of a book along the lines of *New and Non-official Remedies*, published by the Council on Pharmacy and Chemistry. As an illustration of present-day enterprise the article is well worth reading, though the evidence, as presented, is not creditable to the physicians and pharmacists involved.

PHARMACEUTICAL MANUFACTURERS AND THE GREAT AMERICAN FRAUD.—Medical practitioners are beginning to take a greater in-

terest in the source of their medicaments and are taking cognizance of the part taken by pharmaceutical manufacturers in supplying all customers regardless of the use to which their products may be put.

An editorial in the *Journal of the American Medical Association* (July 2, 1910, v. 55, p. 34) in discussing the part taken by many of the larger manufacturers in supplying ready to market products to defraud the sick says: "Legally they may be within their rights but ethically and morally their course is iniquitous, and no amount of argumentative sophistry will justify the attitude of the manufacturing pharmacists who are willing to sell their products to any who will pay for them, no matter to what use the drugs are to be put."

Additional comments will be found in the same *Journal*, v. 55, pp. 40, 418, 613.

SOOTHING SYRUPS AND RETAIL DRUGGISTS.—A decidedly progressive step is evidenced by the resolutions recently adopted by the Philadelphia Association of Retail Druggists, condemning so-called soothing syrups containing morphine and cocaine and refusing to sell them. This action has been commented upon quite widely and it is to be hoped that the association will be successful in its efforts to induce the state legislature, at its next session, to eliminate from statute books the present law which permits the sale of these drugs, providing the objectionable ingredients are announced on the labels (*J. Am. M. Ass.*, 1910, v. 55, p. 607).

EHRLICH-HATA "606," is one of the many designations that have been employed for the substance that is creating unusual attention as a possible specific for a number of diseases that are known to be due to spirochetes. The new remedy promises to be the most valuable discovery in the field of materia medica since the introduction of diphtheria antitoxin. The substance, which chemically is said to be dioxidydiaminoarsenobenzol ( $C_{12}H_{12}O_2N_2As_2$ ), has been selected from a long list of substances that have been experimented with because of their supposed or actual destructive influence on spirochetes, a class of organisms that have been shown to be the causative factors in a number of transmissible diseases. The reported results obtained are all but marvellous and the lay as well as medical journals of Europe are filled with discussions of the possible curative value of the compound.

Ehrlich himself has wisely safeguarded the use of the sub-

stance and is unwilling to allow its commercial exploitation until satisfied that the remedy will prove to be comparatively safe in the hands of the general practitioner. In view of the fact that it is a compound more or less closely allied to arsenilic acid, which in its various forms has been the cause of many cases of blindness, the precaution appears to be exceptionally commendable (*J. Am. M. Ass.*, 1910, v. 55, p. 601, 609, 610).

ALCOHOL A DANGEROUS AND UNNECESSARY MEDICINE.—A book review calls attention to a book with the above title recently published by Mrs. Martha M. Allen, Superintendent of the Department of Medical Temperance for the National Woman's Christian Temperance Union. The book comprises a collection of expressions of opinion by medical writers and is well worth more than casual notice on the part of pharmacists who are anxious to free their calling from the widely made imputation that they are in effect liquor distributors (*J. Am. M. Ass.*, 1910, v. 55, p. 523).

ALCOHOLIC BEVERAGES.—The London correspondent asserts that: "The tendency of recent years has been to limit considerably the field of the utility of alcohol, and the amount consumed in the hospitals is a mere fraction of that consumed a few years ago." A recently issued manifesto signed by 101 physicians in North Wales appeals to medical men to join them in an endeavor to discountenance the popular error that alcoholic drinks are necessary for the promotion of health by refraining from their employment in the treatment of disease (*J. Am. M. Ass.*, 1910, v. 54, p. 2130).

OFFICIAL RECOGNITION OF ALCOHOLIC BEVERAGES is well shown by the following:

TABLE SHOWING THE RECOGNITION ACCORDED TO WINE AND DISTILLED LIQUORS  
IN THE SEVERAL NATIONAL PHARMACOPŒIAS.

	British	German	French	Swiss	Dutch	Austrian	Belgian	Hungarian	Japanese	Spanish	Swedish	Italian	Danish	United States
Brandy .....	+	+	o	+	o	+	o	o	o	o	o	+	o	+
Rum.....	o	o	o	+	o	o	o	o	o	o	o	o	o	o
Whisky .....	o	o	o	o	o	o	o	o	o	o	o	o	o	+
Wine.....	+	+	*	?	+	+	+	+	+	*	+	+	?	+

Pharmacopœias marked + ? contain only a general article on medicinal wines, but no tests for or descriptions of wine itself.

Pharmacopœias marked \* contain a general descriptive article on wine but no standards for any particular kind of wine.

ANTIPIRYN.—G. O. H. Wallace (*Lancet*) records a case of acute poisoning by 10 grains of antipyrin. Within fifteen minutes of taking the drug the patient complained of faintness and suffocation and the face became "blotchy" and swollen. While being examined she suddenly collapsed and became unconscious, but revived, and after treatment in bed for two days recovered. The most marked features of the case were the rapid onset and recovery, a low temperature, and great prostration (*Pharm. J. Lond.*, 1910, v. 85, p. 130).

ANTITYPHOID VACCINATION.—Frederick M. Hartsock, Major, Medical Corps, U. S. Army, reports the results of 1100 inoculations or antityphoid vaccinations by means of the injection of dead typhoid bacilli. This, he asserts, is destined to be a practical measure of prophylaxis and will be particularly useful in the handling of typhoid epidemics. In his experience no untoward results were noted; all patients recovered promptly. Even in the limited number of cases (10) in which the reaction was severe the patients were able to attend to duty after 24 hours (*J. Am. M. Ass.*, 1910, v. 54, p. 2123).

BISMUTH MILKS.—Dr. Judson A. Hulse warns against the use of bismuth preparations in the shape of creams, milks, etc.

In a series of observations covering their administration to 21 infants suffering from acute gastro-enteric conditions, he failed to observe a sedative or astringent action in a single case. In a number of cases the bismuth milk passed through the entire alimentary tract practically unchanged, while in control observations it was found that the administration of bismuth subnitrate resulted in darkened stools, lessened amount of blood, and almost complete disappearance of mucus within the first twenty-four hours of its administration (*J. Am. M. Ass.*, 1910, v. 55, p. 236).

(To be continued.)



# THE AMERICAN JOURNAL OF PHARMACY

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## THE ASSAY OF IODOFORM AND IODOFORM GAUZE.

By A. H. CLARK.

In searching the available literature for a satisfactory method for the determination of iodoform in medicated gauze and also for the assay of iodoform, the method of Uts (*Apoth. Ztg.*, 18, No. 98, Dec. 9, 1903, 869) and that of Gane and Webster (*Merck's Report*, 18, No. 1, p. 13, 1909) seemed to be the most readily applicable.

Uts dissolves the iodoform in spirit of ether, adds fuming nitric acid, an excess silver nitrate V.S., and heats until the odor of nitrous acid has disappeared. The excess of silver nitrate V.S. is then determined with  $\frac{1}{10}$  normal ammonium sulphocyanide V.S.

Gane and Webster dissolve the iodoform in alcohol and ether in the proportion of 3 parts of alcohol to 1 part of ether. Commercial nitrous acid is then added, the mixture heated, and the excess silver nitrate V.S. determined with  $\frac{1}{10}$  normal potassium sulphocyanide V.S. Gauze, lint, etc., are exhausted with ether and the ethereal solution treated as described.

Both methods were found to give excellent satisfaction. In the effort to shorten the method as applied to gauze, I found that it is not necessary to *dissolve* the iodoform in alcohol or ether, neither is the *fuming* nitric acid necessary. Boiling under a reflux condenser for one-half hour in the presence of alcohol and nitric acid, U.S.P., is sufficient to convert all of the iodine to silver iodide. By the use of alcohol alone a simultaneous extraction of the gauze and determination of the iodoform may be carried out, and this much easier than if ether is present. Using ether for

extraction with water present, the temperature of the distilling flask must be carefully controlled or it will rise to such a point that when the ether siphons over and comes in contact with the hot water it will vaporize so rapidly that there is great danger of loss. There is no trouble of this kind if alcohol only is used. The following is the process in detail as finally adapted to the assay of iodoform.

The iodoform is added to 50 c.c.  $\frac{1}{10}$  normal silver nitrate V.S., to which has been added 3 c.c. nitric acid, U.S.P., 50 c.c. alcohol is added, the whole being contained in a 250 c.c. florence flask. The flask is now connected with a reflux condenser and heat applied so that it boils gently. The heating is best conducted by placing the flask in a water-bath so that the water in the bath is about on a level with the water in the flask. This procedure avoids any bumping or spattering. The heat is continued for one-half hour after the boiling commences. After allowing the flask to cool, water is added to make about 150 c.c., a little ferric ammonium sulphate T.S. added, and the excess silver nitrate V.S. determined with potassium sulphocyanide V.S. Each c.c.  $\frac{1}{10}$  normal silver nitrate V.S. is equivalent to 0.0130 Gm. iodoform. The following experiments demonstrate the accuracy of the method.

A sample of iodoform was first procured of good quality and its purity determined by the Carius method. This sample was used in all of the experiments recorded below.

Iodoform taken.	Silver iodide weighed.	Iodoform found.	Per cent. pure.
0.7011	1.2631	0.7048	100.52
0.5352	0.9632	0.5382	100.56

The sample was then assayed by the method as given above.

Iodoform taken.	Iodoform found.	Per cent. pure.
0.3375	0.3386	100.33
0.2011	0.2017	100.29
0.1814	0.1819	100.27
0.2094	0.2095	100.05

The principle is applied to the assay of gauze as follows:

The gauze is placed in a Soxhlet extractor of about 60 c.c. capacity and the entire apparatus connected as usual, except that a

250 c.c. florence flask, containing the  $\frac{1}{10}$  normal silver nitrate V.S. and the nitric acid, is connected with the extraction tube in place of the usual wide-mouth extraction flask. A water-bath is placed so that the flask is immersed in the water as described above. Alcohol is then poured through the condenser onto the gauze in the extraction tube until it siphons into the flask. Heat is then applied to the water-bath until the contents of the flask boil briskly. The extraction is continued for one hour, when the flask is disconnected and, after cooling, the titration made as described above. Experiments were made in which a known weight of iodoform was added to plain gauze and treated as above described. The results follow:

Iodoform taken.	Iodoform found.	Per cent. found.
0.2111	0.2117	100.29
0.1953	0.1952	99.95
0.4336	0.4355	100.45

The method is, of course, open to the objection that in commercial gauze the alcohol might extract substances other than iodoform which will consume the silver nitrate solution, and thus make the result too high. The absence of such substances would have to be demonstrated before the assay is made. The method has given perfect satisfaction in a large number of determinations where the absence of interfering substances was known.

UNIVERSITY OF ILLINOIS SCHOOL OF PHARMACY.

## PHYSIOLOGIC STANDARDIZATION OF CARDIAC STIMULANTS AND DEPRESSANTS.

BY THOMAS S. GITHENS, M.D.

TOGETHER WITH A COMPARISON OF SUCH STANDARDIZATION  
 WITH SOME RESULTS OBTAINED BY CHEMICAL ASSAY.

BY CHARLES E. VANDERKLEED, PHAR. D.

In spite of the large amount of physiologic work which has been done with the vegetable drugs in order to determine the method by which they act and the organs and processes which are first and most markedly affected, we find very little in the literature in regard to determination of the strength of these drugs or the

amount required to produce certain effects. In the text-books on therapeutics we find a distinction drawn between the effects of "small" and of "large" or "toxic" doses on the various animals used for experimental purposes, but very rarely do we find any exact statement as to what amount of the drug per gramme of animal constitutes such a dose.

For this reason it has seemed interesting as well as important to determine the exact amount of various drugs which was required to produce definite effects in laboratory animals and to determine also which method of testing was best suited to each drug.

Commercially this study is of importance on account of the desire of manufacturers of these drugs and their products to put on the market preparations of definite physiologic strength, from drugs the chemical study of which is not a criterion of activity. My studies have been largely limited to such drugs for this reason.

The drugs whose standardization I will consider are apocynum, aconite, convallaria, digitalis, gelsemium, squill, strophanthus, and veratrum. These drugs fall into two groups: those which raise blood-pressure, the so-called digitalis series, apocynum, convallaria, digitalis, squill, and strophanthus; and those which lower blood-pressure, aconite, gelsemium, and veratrum.

We will consider, first, the drugs of the digitalis series. Three methods are available for the purpose of quantitative determination of their activity.

1. The effect on the isolated heart of the frog or turtle.
2. The effect on the blood-pressure.
3. The amount required to cause death.

As the effect on the heart is that which makes these drugs useful in practical medicine, it is often stated that the best method of testing them is directly on the heart. The effect on this organ can be studied to the exclusion of all other factors by the following method: The heart of a frog or turtle will continue to beat, if it is placed in a solution of proper salts, after its removal from the body. If the heart is cut into longitudinal strips, each of these will continue to beat under proper conditions, and may live for two or even three days after removal from the body. It would seem that by adding the drug to be tested to the liquid in which the strips are suspended, the effect of this on the heart itself might be determined with great accuracy. This would be true



but for the fact that organs isolated from the body and kept under artificial conditions are very susceptible to slight alterations in their surroundings,—so much so, that if four strips are cut from the same heart and are kept under apparently identical conditions, they may show great differences among themselves, and although the effect of the addition of a given drug to the solution might easily be seen in the alteration of the rhythm, the differences between the reaction of different strips would be greater than that between different specimens of the same drug. In work of this sort which I have done, I found that the difference in the effect of a given quantity of a drug and twice this amount was not very marked, although there was generally a fairly marked difference between a given amount and four times as much. A method which gives results showing a variation of 50 per cent. in one direction or the other can of course not be depended on for quantitative standardization.

The second method, the effect on the blood-pressure, has also something in its favor, inasmuch as the stimulating effect of these drugs on the heart is in more or less direct proportion to the effect on the blood-pressure. If the effect of drugs on the blood-pressure is studied, it will be found that the rise following an injection is not in proportion to the dose given. A small dose will cause a perceptible rise, but twice this dose will not cause twice this rise. In fact, we find that a certain dose brings about almost a maximal rise and that increasing the dose will merely increase toxic phenomena, so that the pressure will fall more rapidly than after the smaller dose. The effects of large and small doses are thus distinguished with difficulty and the same is, *pari passu*, true of equal doses of strong and weak preparations. It is evident from these facts that if we choose as our standard dose the smallest amount which will bring about a maximum rise, a drug much stronger than our standard will cause much the same rise and will, through its toxic action, cause the pressure to fall sooner than would a weaker preparation, and thus a strong preparation will appear weak instead of strong.

To avoid this tendency to toxic action it will be necessary to give a dose, of the preparation to be tested, so small that there is no danger of overstepping the bounds of normal physiologic action, however strong the specimen in hand. The use of so small a dose betrays us unfortunately from the Scylla of toxic action

to the Charybdis of uncertain reaction. It is a well known fact of physiology, that the stronger the stimulus the more nearly in accord are the results obtained on different individuals. This is particularly true of drug action. If  $\frac{1}{16}$  of a grain of morphine be given to each of a series of persons, it will cause sleep in this person, nausea in that, wakefulness in a third, and perhaps a headache in a fourth. If, however, several grains are given to the same persons, it will cause narcosis in all. The same difference in reaction to small doses of medicine is seen in the effect of blood-pressure-raising drugs on different individuals. For this reason it is necessary to give first to the animals on which the tests are being carried out, a dose of a standard preparation, and then to determine how much of the preparation to be tested is required to bring about the same rise. The elimination of most drugs is so slow as to render this method valueless. With the exception of such drugs as amyl nitrite, which is eliminated within a few minutes, and adrenal principle, which is destroyed as rapidly, the effect of the first dose cannot, under the ordinary conditions of experiment, be allowed to pass off entirely before the next dose is administered, and there is for this reason a cumulative action, each dose adding to the effect of the previous one and rendering a true comparison impossible.

We thus come by a process of exclusion to the third method, the determination of the amount of a drug required to cause death. This amount is ordinarily determined by injecting into a series of animals progressively larger doses of the drug under consideration, and noting the smallest dose required to cause death. The method is therefore known as a minimal lethal (fatal) dose method. A large series of experiments show that by basing the dose on the weight of the animal, the activity of the preparation can be determined to within 10 per cent. That is to say, if a given dose is the smallest which will kill a given animal,  $\frac{11}{10}$  of this amount will kill almost any individual of the same species, and  $\frac{9}{10}$  of this amount will hardly ever kill. This fact bears out what has been said above concerning the agreement in the effects of large doses.

Granting then that the method gives concordant results, can we be at all sure that the toxic power which is estimated in this way is in accord with the therapeutic activity of the preparation? The

physiologic action of these drugs, on which their therapeutic value depends, is mainly a stimulation of the heart, shown by more forcible contraction of its wall. The drugs kill either by inducing a state of constant contraction (death in systole) or by overworking the heart muscle to such an extent that it gives way to a more or less sudden exhaustion with relaxation (death in diastole). In either case, the effect is primarily due to stimulation of the heart, and thus varies in accord with the physiologic or therapeutic activity. In this connection it may be as well to mention that occasionally in mammals, the respiration ceases before the heart has come to a standstill. This does not indicate any direct action of the drug on the respiratory centres, but is due to interference with the function of the medulla, dependent on the disturbance of its blood supply. The death is thus due to the stimulating action on the heart, however it may eventually occur. Granting then that the lethal dose method is not only exact, but also determines the physiologic activity, what animal is the best to use? It is often stated that as the drug acts on the medulla in mammals, as shown by respiration occasionally ceasing before the cardiac contractions, the drugs should be tested on frogs, in which it acts on the heart. As we have seen, the respiratory failure is really due to beginning cardiac exhaustion, and in reality there is no essential physiologic difference between the action of the drugs on the frog and on the guinea pig. The action of digitalis is largely exerted on the cardiac ganglia. In the frog these ganglia are in the heart, as may be demonstrated by the continuance of contractions after the removal of the organ from the body. In birds they are in the spinal cord, as is shown by the cardiac action continuing after the head is cut off. In mammals, however, the cardiac ganglia are in the base of the brain and any stimulus acting on these ganglia acts of course on the brain.

The frog is an unsatisfactory animal for the purpose of standardization, as its reaction to stimulation is markedly influenced by external surroundings, temperature, amount of moisture present in the cage, relation of time of injection to time of feeding, etc. The species of frog also makes a difference and, according to many authors, the time of year. Certain writers believe that season has of itself no influence, but that the differences found are dependent on different species being used, or on temperature. Al-

though the uncertainty arising from these factors may be avoided by great care, there will be a difference in different lots of frogs, and it is recommended by those who used the frog method, that a standard preparation of each drug be kept on hand and that each fresh batch of frogs be studied as to their relation to the standard before they are used for the purpose of testing new preparations. This makes the standard dependent on the keeping properties of a stock galenical, and these are exceedingly uncertain in many drugs. Any deterioration will result in a lowering of the standard for all subsequent preparations. For these reasons it seems wiser to use some animal which shows no such variation, is always of the same species, can be easily obtained, and is large enough to allow accurate and easy calculation and measurement of doses. The guinea pig fulfils all of these requirements, and has therefore been selected by us for use in our experiments. Moreover, as the guinea pig is very resistant to the action of alcohol, it is not necessary to evaporate alcoholic preparations to dryness before injecting them. The necessity for such evaporation when using frogs is of course well known.

It is a noteworthy fact, to which attention has often been directed, that the smaller animals require doses much larger in proportion to their weight. For instance, 0.75 c.c. tincture digitalis which can be given safely to a 250 gramme guinea pig, would correspond to 7.2 oz. to a 150 pound man, which would be far above a fatal dose. It has therefore been proposed that the dose should be based on the relative surfaces of the animals instead of on their weight. This would be the  $\frac{2}{3}$  power of the weight, the square of the cube root. This would give a dose of little more than 1 oz. to a 150 pound man, which is about the largest dose which can be given safely. A series of experiments on guinea pigs of different weight have shown that this argument does not apply to them. Comparing pigs of about 225 grammes weight with others of 500 grammes, we find that upwards of twice as much is required to kill the larger animals. This shows that for animals of the same species the dose should be in proportion to the weight and not in proportion to the surface area.

In doing the routine work of standardization, the guinea pigs are first weighed, and then to one pig is given hypodermically the standard minimal lethal dose, to a second  $\frac{9}{10}$  of this, and to a third  $\frac{11}{10}$ . If the drug is of proper strength, the two pigs



receiving the larger doses will die, while the third will recover. This being the case the drug or preparation may be passed as it is. If only the pig receiving  $\frac{11}{10}$  dies, the preparation is to be concentrated 10 per cent. If all three pigs die, a fresh pig is given  $\frac{8}{10}$  of the standard dose and the dose is reduced by tenths until a pig lives. The preparation is then diluted accordingly. If all three pigs live, a fresh pig is given  $\frac{12}{10}$ , and others increasing doses until two die. The preparation is then concentrated to agree with the smallest amount received by a pig which is killed.

By this method it is possible to make preparations which are always within 10 per cent. of the same strength. The standards on which I have decided, after a large amount of work with preparations from different houses, are as follows:

DOSE BASED ON A 250 GRAMME GUINEA PIG, AND PROPORTIONED TO WEIGHT  
IF THE PIG USED DOES NOT WEIGH THIS.

Drug	Fluidextract	Tincture	Extract
Apocynum .....	0.075 c.c.	0.75 c.c.	
Convallaria .....	0.075 c.c.	0.75 c.c.	
Digitalis .....	0.1 c.c.	1.0 c.c.	0.025 Gm.
Squill.....	1890		
	0.25 c.c.		
	1900		
	0.5 c.c.	0.75 c.c.	
Strophanthus .....	0.0025 c.c.	0.025 c.c.	

The most interesting point in connection with this table is the peculiar difference in the activity of the three preparations of squill. The alcoholic extract is about twice as strong as the acetic, or a little more, and the tincture about three times as active as the alcoholic extract, in proportion to drug strength.

We now turn to the consideration of the *heart depressants*. There are only three vegetable drugs in the Pharmacopœia whose most important physiologic action is a direct depression of the cardiac activity,—these being aconite, gelsemium, and veratrum. Related to these in action is a group of drugs which exert their most marked action on the voluntary muscles, causing loss of tone in these, and killing by respiratory, rather than cardiac, failure. This group includes physostigma, lobelia, and conium. The drugs of the digitalis series, which kill by depression resulting from over-

stimulation, show a very sharp line between their therapeutic and toxic doses. A dose slightly less than that which is required to cause death causes only slight toxic phenomena. With the drugs of this class, on the contrary, the toxic symptoms are manifested even under the influence of comparatively small doses and these increase gradually until death is reached. For this reason, the dosage of these drugs is not as sharply defined as that of the drugs previously considered, and it is necessary, in making a standard for these drugs, to arbitrarily fix a period of time within which the animal must die, if the drug is to be considered up to standard. This period has been fixed as three hours, as we have found that ordinarily a dose which will eventually prove fatal will do so within this time.

The *heart depressants* differ from the drugs of the digitalis series in another respect, each of them producing evident effects when given in sublethal doses. Aconite causes in many cases nausea, which is shown in the guinea pig by violent retching. As far as our observations are concerned, this animal never vomits. The irritant effect is also shown by the tendency of this drug to cause diarrhœa.

Gelsemium is likely to cause convulsions and these are frequently followed by paralysis, even in cases in which the animal eventually recovers. The guinea pig poisoned with gelsemium lies on the side, moving the legs feebly from time to time and breathing irregularly, and frequently only at long intervals. This paralysis may not come on until an hour or so after the administration of the drug, and in this case, recovery is likely to take place. If the paralysis occurs within twenty minutes of the time the drug is administered, the dose will generally prove fatal.

Veratrum stands between aconite and gelsemium in regard to these phenomena, causing convulsions less frequently than the latter, but being very likely to cause paralysis. Retching and diarrhœa, although not so common as with aconite, are frequently seen. It might be mentioned in this connection that, of the drugs spoken of in the previous article, apocynum frequently causes paralysis, even in animals which eventually recover, and squill and convallaria often cause convulsions. Digitalis is much freer from these sublethal toxic phenomena.

The drugs which have been mentioned as causing death by failure of the respiration can all be standardized by chemical means,

as their activity is largely dependent upon their alkaloidal content. Although aconite, gelsemium and veratrum contain alkaloids upon which their activity depends, their physiologic strength does not necessarily nor invariably vary in accordance with their alkaloidal content. The physiologic activity of aconite is mainly due to the aconitine which it contains, but this alkaloid contains in chemical combination a methyl and a benzoyl group, either of which may be split off during the handling of the drug and the loss of which renders the aconitine inactive, while still permitting it to respond to the chemical reactions of an alkaloid. This is particularly prone to occur on long standing of its preparations. Veratrum contains, in addition to veratrine, a series of alkaloids, among which may be mentioned protoveratrine, veratroidine and protoveratridine, which are almost entirely inactive, but which cannot be easily distinguished chemically from the active alkaloids. Gelsemium contains two alkaloids, gelsemine and gelseminine, the former of which has practically no effect on mammals but cannot well be distinguished by any chemical assay process. On account of the possibility, therefore, of obtaining misleading results from chemical assay alone, we are reduced to the necessity of substantiating such assays by physiologic means. Conium, physostigma, and lobelia all contain alkaloids upon which their pharmacologic and therapeutic activity depends, and the amount of which gives a direct indication of the therapeutic activity of the product. It is therefore not considered necessary to standardize these products physiologically.

After a large number of experiments extending over several months, the following standards have been adopted for the three drugs first mentioned. In each case the amount mentioned is injected subcutaneously into a guinea pig, and other pigs are given respectively  $\frac{9}{10}$  and  $\frac{11}{10}$  of the standard dose. If all three of these doses prove fatal, a smaller dose is given to a fresh pig; if none prove fatal, a larger dose is given to a fresh pig. If the dose given in the table proves fatal within three hours, and the pig receiving  $\frac{9}{10}$  of this lives longer than this period, the drug is considered to be of standard quality. The doses given in the table are based on 250 gramme pigs and in case the pig weighs more or less than this amount, are made proportionate to its weight. The dosage is given in grammes of the drug and extract and in cubic centimetres of the liquid preparations.

Preparation	Drug	Fluidextract	Tincture	Extract
Aconite root .....	0.0100	0.0100	0.100	0.002
Aconite leaf .....	0.0150	0.0150	0.150	0.00375
Gelsemium .....	0.25	0.375	2.5	0.100
Veratrum .....	0.05	0.05	0.5	0.015

Feeling that perhaps the standard lethal doses of the drugs referred to in this paper might be more clearly understood if they were stated in a manner similar to that in use in describing the strength of bacterial toxins,—that is, by stating the number of units contained in a cubic centimetre of a standard preparation, we suggest the following system, namely, that the unit in this case be the amount required to kill one gramme of animal (guinea pig). By this method of calculation we have prepared the following table:

Preparation	Drug	Fluidextract	Tincture	Extract
Aconite root .....	25,000	25,000	2,500	125,000
Aconite leaf .....	16,600	16,600	1,660	66,000
Apocynum .....	3,300	3,300	330	
Convallaria .....	3,300	3,300	330	
Digitalis .....	2,500	2,500	250	10,000
Gelsemium .....	1,000	660	100	2,500
Squill.....		<div style="display: inline-block; vertical-align: middle;"> <div style="display: inline-block; vertical-align: middle;"> 1890 1000 1900 500 </div> </div>	330	
Strophanthus .....	100,000	100,000	10,000	
Veratrum .....	5,000	5,000	500	16,600

Of the drugs tabulated in the preceding portion of this communication only the following are sufficiently accurately provided with *chemical assay processes* to enable us to make comparisons: digitalis; aconite root; aconite leaf; gelsemium; veratrum.

*Digitalis*.—Attention is first called to the article by Reed and Vanderkleed on the standardization of digitalis preparations, published in the March, 1908, number of the AMERICAN JOURNAL OF PHARMACY. There, on page 119, is given a table showing the relationship between chemical assay for digitoxin and physiologic assay based upon lethal dose for guinea pigs, for nine preparations. During the past year, the results as shown in the following table indicate that the minimum lethal doses as obtained by Dr. Reed two years ago were slightly smaller than those obtained by Dr. Githens during the past year, when compared with the results



obtained by chemical assay as described in the article mentioned above.

No.	Preparation	Chem. Assay Gramme Digitoxin in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Per cent. Digitoxin Calculated from a Lethal Dose of 1 c.c. of Tinct.
1	Tinct. U.S.P. ....	0.0326	0.8 c.c.	0.02608
2	Tinct. U.S.P. ....	0.0329	0.8 c.c.	0.02630
3	Tinct. U.S.P. ....	0.0290	1.0 c.c.	0.02900
4	Tinct. U.S.P. ....	0.0280	1.1 c.c.	0.03080
5	Tinct. U.S.P. ....	0.0380	0.9 c.c.	0.03420
6	Tinct. Fat free .....	0.0410	0.9 c.c.	0.03690
7	Tinct. Fat free .....	0.0328	1.1 c.c.	0.03690
8	Tinct. Fat free .....	0.0375	0.9 c.c.	0.03375
9	Tinct. Fat free .....	0.0440	0.75 c.c.	0.03300
10	Tinct. Fat free .....	0.0240	1.25 c.c.	0.03000
11	Tinct. Fat free .....	0.0365	0.8 c.c.	0.02920
12	Tinct. Fat free .....	0.0290	1.0 c.c.	0.02900
13	Powdered Ext. ....	0.763 per cent.	0.031 Gm.	0.02370
Average .....				0.03061

A study of the table of March, 1908, shows that an assay of about 0.025 Gm. digitoxin per 100 c.c. corresponded closely with a lethal dosage for 240 Gm. guinea pigs of about 1 c.c. A careful scrutiny of the above results shows not quite so uniform an agreement, but, on the whole, a minimum lethal dose of 1 c.c. corresponds fairly closely with an assay of 0.030 Gm. digitoxin per 100 c.c. The third column, consisting of figures representing the products obtained by multiplying together the figures in columns 1 and 2, shows how nearly concordant the results obtained ran, and corresponds to percentage of digitoxin *calculated from* a lethal dosage of 1 c.c. of tincture, 0.1 c.c. of fluidextract, or 0.025 Gm. powdered extract. The average of this column is 0.0306. Continued work on this interesting assay has shown that the purity of the crystalline digitoxin obtained depends largely on the manipulation of the bulky lead subacetate and sodium phosphate precipitates (see AMER. JOUR. PH., 1908, p. 118). A centrifuge is now being installed in our laboratory suitable for sedimenting these preparations,—and by its use, it is hoped that a higher degree of purity of the separated digitoxin will be obtained, insuring results still more nearly concordant with physiologic assay.

*Aconite Root and Leaf.*—The chemical assay methods employed for all aconite preparations in the following table were essentially those of the U.S.P.

No.	Preparation	Chem. Assay Gramme Aconitine in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Percent. Aconitine calc. from a Lethal Dose of 0.1 c.c. of Tincture
1	Tinct. U.S.P. ....	0.0411	0.130 c.c.	0.053
2	Tinct. U.S.P. ....	0.0614	0.075 c.c.	0.046
3	Tinct. U.S.P. ....	0.0480	0.100 c.c.	0.048
4	Tinct. U.S.P. ....	0.0425	0.125 c.c.	0.053
5	F. E. (leaf).....	0.2400	0.020 c.c.	0.048
6	F. E. (root).....	0.4400	0.0075 c.c.	0.033
7	F. E. (root).....	0.4150	0.0075 c.c.	0.031

Average .....0.044

A survey of the above table shows far less concordance between chemical assay and lethal dose than in the case of digitalis. The agreement is fairly close in the case of the tinctures and of the fluidextract of leaf, but the two fluidextracts of root possess a degree of toxicity about 25 per cent. greater than should have been expected from the chemical assay. A continuation of the collection of data will throw additional light on this peculiar observation.

*Gelsemium*.—A comparison of the results of chemical assay for total alkaloids in gelsemium with its minimum lethal dose was first undertaken at the suggestion of Prof. L. E. Sayre, who describes the results first obtained on page 855 of the 1908 Proceedings of the American Pharmaceutical Association. Attention is also directed to the reported discussion on Prof. Sayre's paper on pages 851-8 of this volume. The following table shows the results obtained since that time,—the chemical assay method used being that of Webster as described by Sayre in the article mentioned above:

No.	Preparation	Chem. Assay Gramme Alkaloid in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Percent. Alkaloids calc. from a Lethal Dose of 0.375 c.c. of Fluidextract
1	Tincture .....	0.0316	2.00 c.c.	0.17
2	Tincture .....	0.0715	1.25 c.c.	0.23
3	Tincture .....	0.0538	2.00 c.c.	0.29
4	Fluidextract .....	0.400	0.375 c.c.	0.40
5	Fluidextract .....	0.400	0.375 c.c.	0.40
6	Fluidextract .....	0.400	0.375 c.c.	0.40
7	Fluidextract .....	0.500	0.300 c.c.	0.40
8	Fluidextract .....	0.550	0.3 c.c.	0.44
9	Fluidextract .....	0.465	0.4 c.c.	0.50
10	Solid extract.....	2.185 per cent.	0.09 Gm.	0.52

Average ..... 0.375

Average on fluid and solid extracts alone ..... 0.437

This table serves to demonstrate the necessity for physiologic control of the chemical assay for gelsemium and the worthlessness of the latter unless accompanied and checked by the physiologic test. Just contrary to the results obtained with aconite, the *tinctures* of gelsemium are much more toxic than the fluidextracts, on the basis of equivalent amounts of total alkaloid. This is probably due to a higher proportion of highly active gelseminine being taken up by the prolonged percolation which occurs in the preparation of the tincture.

*Veratrum*.—The chemical results, expressing total alkaloids, in the following table were obtained by the following method:

The fluidextract, 10 c.c., or the tincture, 100 c.c., is evaporated on purified oak sawdust, and the dried mixture macerated with a mixture of ether, 80 c.c., chloroform, 20 c.c., and ammonia water, 10 per cent.—10 c.c. An aliquot part of the ethereal extract is shaken out with 5 per cent. acetic acid, rendered alkaline with ammonia, shaken out with chloroform, evaporated, dried, and weighed.

In the case of the solid extract, 2 or 3 grammes are dissolved in 50 per cent. alcohol, filtered onto purified oak sawdust, and finished like the fluidextract and tincture.

No.	Preparation	Chem. Assay Gramme Alkaloid in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Percent. Alkaloids calc. from a Lethal Dose of 0.5 c.c. of Tincture
1	Tincture .....	0.1	0.5 c.c.	0.100
2	Tincture .....	0.102	0.5 c.c.	0.102
3	Tincture .....	0.078	0.75 c.c.	0.117
4	Solid extract .....	4.0 per cent.	0.015 Gm.	0.120
5	Fluidextract .....	1.0	0.05 c.c.	0.100
6	Fluidextract .....	1.145	0.065 c.c.	0.149
Average .....				0.115

Except for No. 6 in the above table, the lethal dose of which is abnormally high in comparison with the chemical assay, the activity of preparations of veratrum seems to agree quite closely with the percentage of total alkaloids. The chemical assay of veratrum appears therefore to possess undoubted value.

It is the intention of the authors to continue the tabulation of comparative results of physiologic and chemical assay of these drugs, as well as to start similar series of comparisons on conium, physostigma, and lobelia.

RESEARCH LABORATORIES OF  
 H. K. MULFORD COMPANY.

A CONTRIBUTION TO THE HISTORY OF  
" PINK-ROOT." \*

BY M. I. WILBERT.

*Spigelia marilandica* illustrates, as well perhaps as any drug now used, the interesting comedy of errors that may be developed by following up the history of the origin and uses of a drug that has passed through the vagaries incident to its empiric use in medicine.

Much of the confusion concerning this particular drug, and its adulterant, has been unravelled by W. W. Stockberger in his comprehensive and scholarly monograph on "Pink-root and its Substitutes," published in part as Bulletin 100 of the Bureau of Plant Industry and in full in the *Pharmaceutical Review* for 1907, also as a separate by the Pharmaceutical Review Publishing Co., Milwaukee, 1907.

Stockberger, however, leaves two rather interesting questions unanswered, at least directly: (1) Who was the first to recognize the then common adulterant of spigelia as *Phlox carolina*? (2) What was the nature of the second "pink-root" frequently referred to as having been in use in this country during the earlier decades of the nineteenth century?

I believe that the direct answer to the first question is to be found in one of the very few references that Stockberger appears to have overlooked in the compiling of his admittedly comprehensive bibliography of the literature on "pink-root."

The first edition of the National Dispensatory (1879) in the monograph on spigelia, evidently written by Maisch, says: "Spigelia is sometimes met with as an admixture of serpentaria, and is not infrequently found mixed with some few roots of several plants, doubtless from careless collection. A few years ago a very different root was seen in the market, which Dr. A. W. Miller (1875) ascertained to have been derived from *Phlox carolina*, Lin., which plant is known in some parts as Carolina pink. This root is lighter in color, the rootlets are straight or but slightly curved, and their cortical portion is easily removed, exposing a straw colored ligneous thread."

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\* Presented at the Historical Section, A. Ph. A., 1909.



The first announcement of this adulterant appears to have been made at a pharmaceutical meeting of the Philadelphia College of Pharmacy, February 16, 1875, when "Dr. Miller presented a sophistication of spigelia, to which his attention was drawn by S. W. Brown of Manayunk. Upon inquiry he learned it was known in the market as East Tennessee pink-root; but the plant from which it is derived has not been ascertained. It is said to be largely sold to manufacturers of fluidextracts."

At the annual meeting of the American Pharmaceutical Association, in Boston, in 1875, Dr. A. W. Miller, as chairman of the committee on adulterations and sophistications, presented the final report, quoted by Stockberger, in which he gives a more detailed account of the adulterated pink-root and records securing an additional supply of this "so-called East Tennessee pink-root" from a commission merchant in Philadelphia.

Miller also reports addressing a letter of inquiry to Messrs. Wallace Bros., of Statesville, North Carolina, who "have since been able to identify the sample as the root of *Phlox carolina* known with them as the Carolina pink."

From the available publications it would appear that the adulteration was brought to the attention of Dr. A. W. Miller by S. W. Brown, of Manayunk, and that Dr. Miller submitted samples of the root to Wallace Bros., who identified the same as *Phlox carolina*.

It is quite likely that the claim recorded by Stockberger as having been made by M. E. Hyams is correct, as a personal letter recently received from Dr. A. W. Miller recalls that a Prof. Hyams was formerly in the employ of Wallace Bros. or affiliated with them as botanist, and it is quite probable that the inquiry from Philadelphia was submitted to him so that the sequence would be complete and Prof. M. E. Hyams really the first to mistake, as True and others have pointed out, *Ruellia* as *Phlox*.

An even more interesting question is the one as to the identity of the second pink-root used in Eclectic and to some extent also in domestic practice during the earlier decades of the nineteenth century.

Dr. Benjamin Smith Barton, in his "Collections for an Essay Towards a Materia Medica of the United States," says: "The *Silene virginica* or ground pink, as it is called in some parts of our country, is another native anthelmintic. A decoction of the root

is used and is said to have been found a very efficacious remedy." In a footnote Barton says: "From the information of my friend, the late Dr. James Greenway, of Virginia."

Dr. John Redman Coxe in the early editions of the American Dispensatory says: "*Silene virginica*, ground pink. This species of silene or catchfly is abundant in many parts of the United States. Some of the Indians say it is a poisonous plant. In decoction the root has been found to be an efficacious anthelmintic."

Many other early writers on American materia medica mention this particular member of the pink family which appears to have met with some use both at home and abroad and may, in part at least, account for the practice observed by Flückiger and Hanbury who note that spigelia or pink-root is sometimes erroneously latinized in price lists as "*Radix Caryophylli*."

In some of the early Eclectic works on materia medica, *Silene virginica* was recommended as a vermifuge and a nervine. It was popularly known as "wild pink, pink catchfly, fire pink, ground pink, and Virginia pink." No reference to the use of this root could be found in recent literature and an inquiry addressed to some of the larger herb dealers in the country failed to find a single one who had any knowledge of the drug or its uses, and practically the only available reference to it, of recent date, is the continuation of a rather misleading notice in the United States Dispensatory.

The earlier editions of the United States Dispensatory say: *Silene virginica*, catchfly, wild pink, an indigenous perennial plant growing in Western Virginia and Carolina, and in the States beyond the Alleghany Mountains. Dr. Barton in his "Collections" states that a decoction of the roots is said to be efficacious as an anthelmintic. We are told that it is considered poisonous by some of the Indians. The *S. pennsylvanica* which grows in the eastern section of the Union from New York to Virginia probably possesses similar properties.

The 19th edition of the United States Dispensatory (1907) says: *Silene*—*Silene virginica* L. (Fam. Caryophyllaceæ), catchfly, wild pink. The wild pink of West Virginia and the Carolinas was considered by the Indians poisonous and by Barton an anthelmintic.

The latter description is short, positive, and pithy, and is evidently the product of shears and blue pencil, but would it not be more in keeping with a book of reference to delete it entirely or to reconstruct it and allow it to appear as a memorial of a one

time popular remedy, that as Hollembaek and others assert, was frequently employed as a substitute for the *Spigelia marilandica*?

And this suggests that ponderous tomes like the United States Dispensatory frequently contain much that is interesting and amusing, if recognized, and sadly misleading if one unwittingly relies on them for the information that they are expected to contain. Reverting for a moment to spigelia, it will be worth while to read Stockberger's monograph on this drug and then to peruse the peculiar conglomerate of old and new that is presented in the United States Dispensatory as a description for the same.

Among the interesting pieces of information still offered that had their origin before the Civil War, probably before the introduction of railways, is the reference to the emigration of the poor Indian and the marketing of spigelia in huge casks or bales, from St. Louis by way of New Orleans, and the added piece of information that "That contained in casks is to be preferred, as less liable to be damp and mouldy."

Another interesting bit of information is the assertion that: "It is frequently necessary to separate the spigelia from the various adulterant roots. Among the most important of these may be mentioned the roots of certain small vines which frequently twine around the spigelia stem; these roots can be distinguished by their being long, slender, crooked, yellowish, thickly set with short capillary fibres, and much smaller and lighter colored than is pink-root."

This statement is evidently taken from a book by James Ewell, physician in Washington, formerly of Savannah, who early in the nineteenth century expressed the belief that the deleterious effect of commercial spigelia was due to the root of this particular vine.

John Redman Coxe, in the 9th edition of the American Dispensatory, refers to this statement made by Ewell and quotes a letter from a Mr. Porcher, who controverts the theory and quotes a Mr. Stephen Elliot as being of the opinion that the poisonous property observed is characteristic of spigelia itself.

It would appear desirable that, granting that "commentaries" are to be simple compilations, they be so labelled and that wherever possible the original reference or the approximate date be appended so as to give at least some indication of the reliability of the information offered.

THE HISTOLOGY OF THE RHIZOME AND ROOTS OF  
PHLOX OVATA L. (PHLOX CAROLINA L.).\*

BY HENRY KRAEMER.

For some time I have felt the importance of making studies of the structure of the underground portions of American plants, as there are so many vegetable fragments of unknown origin in many cases which are found admixed with the more common drugs, and which have a superficial resemblance to them. Thus, unless careful garbling is practised, these foreign plant parts may not only be found as an admixture, but as an entire substitute for the genuine drug.

My interest in *Phlox carolina* dates back some twelve years when, at my request, Mr. C. D. Beadle, of the Biltmore Herbarium, sent me a number of plants which he collected in the mountains of North Carolina. While I did not make an extended study of the material at the time, I examined it sufficiently to lead to the conclusion<sup>1</sup> that the material which Greenish described in his paper did not answer to the description of *Phlox carolina*. My main object at that time was to determine the origin of a substitute for *Spigelia*, in which one of my students at Northwestern University discovered by accident the presence of calcium carbonate. This substitute was shown subsequently and independently by Stockberger<sup>2</sup> and Holm<sup>3</sup> to be the rhizome of *Ruellia ciliosa*.

In connection with their studies on *Spigelia marilandica* and *Ruellia ciliosa*, these authors have also described the structure of *Phlox ovata* (*Phlox carolina*). While the papers of Stockberger and Holm are excellent contributions to the subject, there are still some features which should be brought out more distinctly, especially from the practical pharmacognostic point of view. Stockberger considers that the rhizome and roots of *Phlox ovata* "rarely or never occur as a substitute for *Spigelia*," and I agree with him in a measure, but its occurrence is still reported and, besides, workers do not seem to be clear in regard to the characters of the drug. I do not, however, agree with the statement made by Stockberger that "the root so generally described and studied as

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\* Read before the Scientific Section of the American Pharmaceutical Association, May, 1910.



*Phlox* must be referred to *Ruellia*," which latter drug I hope to take up later.

In order that errors may be eliminated from the literature, it should be pointed out that in the English translation of Solereder's "Systematic Anatomy of the Dicotyledons," which appeared as recently as 1908, the translators continue the mistake in the original German edition of accepting as true the description given by Greenish <sup>4</sup> of what he had reason to suppose was *Phlox carolina*, but which it has since been seen was not an authentic specimen. It should also be pointed out for the benefit of practical workers that the material studied by Professor Greenish was drug material, some of which was supplied by Professor Maisch, but neither of them is open to criticism, both of them having accepted as probably genuine what was supplied them, as was then more customary. Indeed, Professor Greenish did a very excellent piece of work, and nothing would have been left to be desired if he had known the name of the plant from which the material with which he worked was derived and had named his paper accordingly, that is, by substituting the name *Ruellia ciliosa* for *Phlox carolina*. Later experience also shows that it is extremely hazardous to base a study of a vegetable drug on the commercial material alone, and that no studies of this kind can be considered entirely reliable or authoritative which are not based upon material collected from or compared with that derived from plants which have been identified.

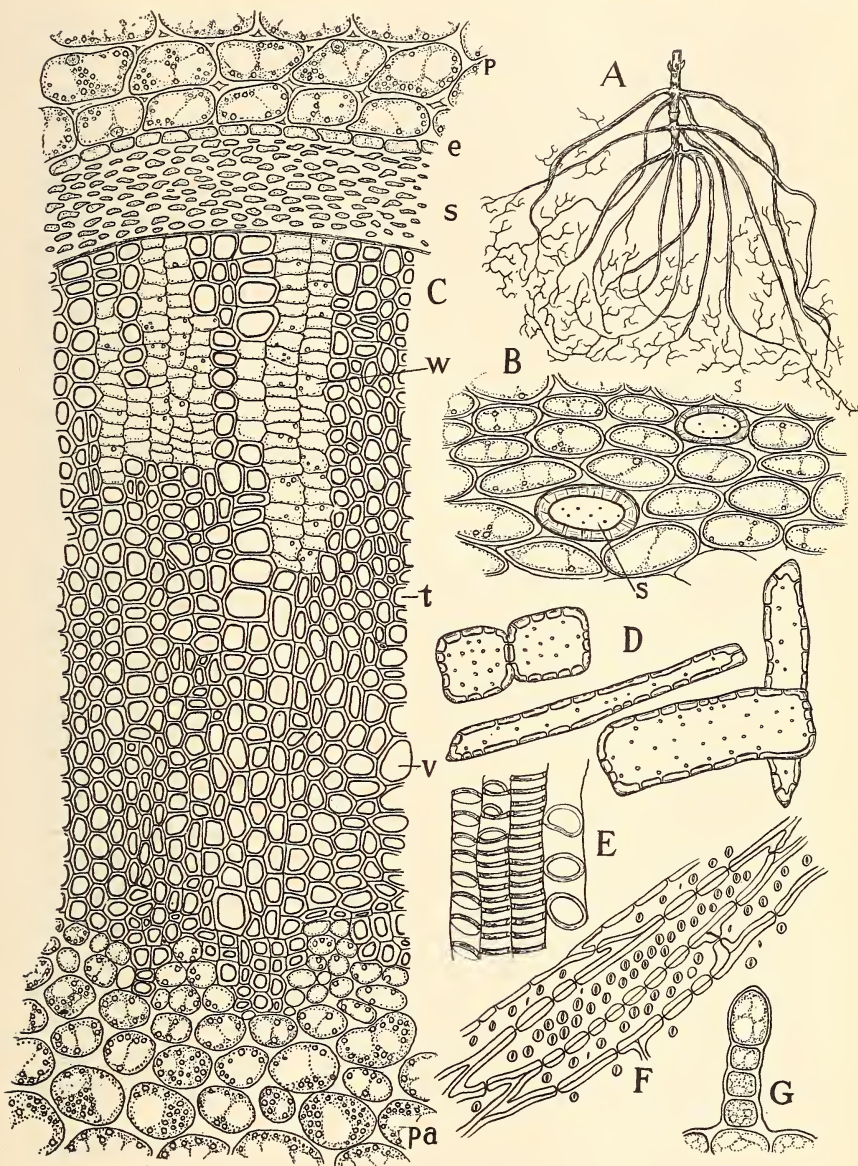
The species belonging to the genus *Phlox* are found chiefly in North America, where they number about thirty. The plants are mostly herbaceous perennials, a number of the species being extensively cultivated for ornamental purposes. The stems are either decumbent or ascending, or in some cases they are slightly decumbent near the base and then ascending, as in *Phlox ovata*. *Phlox ovata* is found in open mountainous woods from Alabama to Pennsylvania, and there are some colored plates representing this plant in the *Botanical Magazine* (t. 528 and 1344). According to Gray, in his "Flora of North America," *Phlox carolina* is merely a taller form of *Phlox ovata*, but having narrower, more tapering leaves and pointed calyx teeth, approaching *Phlox glaberrima*. According to botanists to-day, the form with ovate or ovate-lanceolate leaves is regarded as the typical species, and the name *Phlox carolina* has been superseded by *Phlox ovata*.

*Phlox ovata* generally attains a height of from 3 to 6 decimetres.

The stems are cylindrical, smooth, and the diameter is from  $2\frac{1}{2}$  to  $3\frac{1}{2}$  mm. Thus, they are seen to be slender stems, and in order to maintain their perpendicular position would need to be quite woody, especially in the lower portion, which they are. The so-called rhizome, which is merely an extension of the over-ground stem, is usually vertical, comprising from two to four nodes, and usually 1 to 2 cm. long. From the nodes arise from two to four comparatively thick roots, which are sometimes nearly 2 mm. in diameter in the fresh state, from 1 to 2 decimetres long, unbranched, and produce a large number of fine rootlets, especially near the free ends (Fig. A). The commonly vertical character of the rhizome of *Phlox ovata* is one of the features which distinguishes it from the rhizomes of both *Spigelia* and *Ruellia*, although it should be stated that occasionally decumbent stems are found which produce roots at the nodes. In neither case is that part of the stem producing roots a true rhizome.

The rhizome, or underground part of the stem, is characterized by a strong development of woody tissue, which in transverse section occupies about one-half of the radius. The bark is about 0.5 mm. in diameter, the xylem and phloem together are about 0.9 mm. in diameter, and the radius of the pith is 0.3 mm.

HISTOLOGICAL CHARACTERS OF RHIZOME.—The epidermis in transverse section is made up of rounded tabular cells and is surrounded by a cuticle which is more or less lignified and 8 to 10 microns in thickness. Beneath the epidermis are two to four rows of collenchymatous cells, the remainder of the cortex being made up of about twelve rows of parenchyma cells, the walls of which are about 5 microns thick, the cells themselves being from 40 to 80 microns in diameter. All of the cells of the cortex are rich in protoplasmic contents, and sometimes contain a considerable number of small starch grains, 1 to 3 microns in diameter. Beneath the cells of the cortex there is usually a well-defined ring of endodermal cells, which may be more or less lignified, and which may also contain a few small starch grains. Beneath the endodermis is a layer of pericambial cells, which show one or two tangential divisions. Next beneath is the sieve, which is made up either of thin-walled, somewhat tabular cells, or of oval, very thick-walled cells. The sieve cells are rich in protoplasmic contents, and frequently contain a number of starch grains. The xylem portion of the fibrovascular bundles (Fig. C) is made up of at least two,



*Phlox ovata* L. (*Phlox carolina* L.): A, lower portion of plant showing long roots with numerous rootlets at the ends; B, parenchyma from cortex of rhizome showing two sclerotic cells (s); C, cross-section of portion of rhizome showing parenchyma of cortex (p) which contains protoplasm and starch grains, endodermis (e), leptome (s), tracheae (v), libriform (t), wood parenchyma (w), parenchyma of pith containing starch grains and protoplasm (Pa); D, isolated sclerotic cells from cortex; E, vessels with annular and spiral thickenings; F, libriform cells; G, glandular hair from the leaf.



and frequently three areas—an outer layer composed of compact, strongly lignified cells, which are present in more lignified stems but not here illustrated; a middle layer, as in Fig. B, in which there are radial rows of parenchyma cells separating the thick-walled, lignified cells; and a continuous zone of lignified cells, as in Fig. C. The tracheæ are marked with bordered pores, and those near the centre of the rhizome have annular and spiral markings, the number of tracheæ thus marked being rather striking and characteristic. Most of the lignified cells of the xylem are in the nature of tracheids, which are narrower and longer than those in *Spigelia*, being usually not more than 20 microns in diameter and about 500 microns long (Fig. F). The parenchyma cells in the outer layers of the wood not infrequently show the presence of a number of small starch grains similar to those already described. Underlying the xylem tissue somewhat tabular cells, resembling those of the sieve, sometimes occur, but for the most part all of the cells beneath the xylem, constituting the pith, are made up of somewhat thick-walled parenchyma cells resembling those of the cortex. The walls of these cells are non-lignified, and are wanting in simple pores. The cells are rich in protoplasmic contents, and may contain a large number of starch grains.

The most characteristic features of the rhizome of *Phlox ovata* may be enumerated as follows: (1) The upright or vertical position of the rhizome; (2) the few rather long and comparatively thick roots extending from the nodes; (3) the comparatively thick xylem; (4) the absence of an internal phloem, the fibrovascular bundles being of the collateral type, and (5) the presence of starch in at least the rhizomes of the fruiting plants. The fact that neither Stockberger nor Holm found starch in this rhizome is probably due to their having worked with material in which it was present in rather small quantities, the amount varying unquestionably with the season of the year. I especially mention this point, in view of the fact that Stockberger places *Phlox* in a group in which starch is wanting, and calls attention to its supposed absence as a differentiating character.

The tendency of this plant to produce mechanical cells is further shown by the fact that some of the cells of the pith as well as of the cortex are thick-walled, strongly lignified, the walls being marked by rather fine simple pores (Figs. B, D). These cells as they occur in the pith are either cubical, or elongated and with square ends, while those in the cortex are narrow, with



pointed or oblique ends, and from 100 to 300 microns in length. Somewhat similar stone cells are found in the stem of *Phlox pilosa* L. If the material containing these cells should be relatively abundant in a mixture, their presence would give another character for distinguishing the rhizome of *Phlox* from that of *Spigelia*. The stone cells in *Ruellia* are different in shape, and in addition are associated with cells containing calcium carbonate. The presence of these special, thick-walled lignified cells in the rhizome of *Phlox* may, however, be of infrequent occurrence, like the bast fibres in belladonna, which I have only occasionally seen, but which have been described by Schrenk, and therefore may not be of assistance in the identification of the drug. It might be mentioned in this connection, however, that groups of bast fibres have been found in *Phlox aristata* Michx., and a ring of bast fibres in the stem of *Phlox longifolia* Nutt., *P. Douglassi* Hook., and *P. acuminata* Pursh.

HISTOLOGICAL CHARACTERS OF ROOT.—A transverse section of the root shows (1) ordinary epidermal cells with root-hairs; (2) a hypodermis made up of radially elongated, more or less pentagonal cells; (3) a cortex, consisting of 12 to 20 rows of ellipsoidal rather thin-walled parenchymatous cells, which are rich in protoplasm and may contain small starch grains; (4) a peripheral layer of the central cylinder; (5) endodermis; (6) internal layer of cortex, and (7) within this there is in the very young roots a triarch to pentarch radial fibrovascular bundle, which later becomes collateral and closely resembles in structure that of the rhizome.

While the stem is free from hairs the leaves have rather striking glandular hairs (Fig. G), which are found on the principal veins near the base of the leaf. The histological characters of the leaf have been very well given by Holm, and it therefore does not seem necessary to consider them here.

I may say in conclusion that I am engaged in the study of the structure of the underground parts of other species of *Phlox*, as possibly the rhizomes and roots of other species may occur as admixtures in drugs, and besides the genus is of great interest botanically.

#### LITERATURE CITED.

- <sup>1</sup> Kraemer: "A Course in Botany and Pharmacognosy," 1902, p. 157.
- <sup>2</sup> *Pharmaceutical Review*, 25, pp. 2, 33, 65, 97 (1907).
- <sup>3</sup> AM. JOUR. PHARM., 78, p. 553; 79, p. 51 (1907).
- <sup>4</sup> *Pharm. Jour. and Trans.*, 21, p. 839 (1891); AM. JOUR. PHARM., 63, p. 226 (1891).

## OIL OF SESAMUM—ITS USE IN PHARMACY.\*

BY OTTO RAUBENHEIMER, PH.G., Brooklyn, N. Y.

Oleum sesami, sesame oil, benne oil, gingelli oil, gingelly oil, or teel oil is the fixed oil expressed from the seeds of *Sesamum indicum* L. (Fam. Pedaliaceæ). The sesame plant is indigenous to India, but is largely cultivated also in China, Japan, and most Oriental and tropical countries. According to Miss Alice Henkel, assistant in drug plant investigations, Bureau of Plant Industry, U. S. Department of Agriculture, sesame has also been cultivated to some extent in the Southern States and is said to run wild in the extreme south. The yield of oil is from 47 to 57 per cent. It has a pale yellow color, is nearly inodorous, and has a bland nut-like pleasant taste.

TABLE OF CONSTANTS: Specific gravity at 15° C., 0.920–0.924; specific gravity at 98° C., 0.867–0.870; solidifying test, 4° C.; iodine value, 103–112; and saponification value, 189–193.

Optical rotation, slightly dextrogyrate, + 1 to + 9. The latter is due to sesamin  $C_{18}H_{18}O_5$  and phytosterol. Sesame oil consists essentially of the glycerides of oleic and linoleic acids, with small proportions of stearin, palmitin, and myristin. The two principal advantages of oil of sesamum are that it is a non-drying, or rather a semi-drying oil and that it does not readily turn rancid. The best qualities are largely used in the manufacture of oleo-margarine.

## OLEUM SESAMI SUPERIOR TO COTTONSEED AND OLIVE OILS.

It is official in most of the foreign pharmacopœias and has been admitted to the recently published pharmacopœias, replacing olive oil in a great many galenical preparations. As it is recognized by the *Eragazungsbuch* (supplement to the German Pharmacopœia), it will undoubtedly become official in the new (5th) edition of the *Arzneibuch*.

The colonial addendum of the British Pharmacopœia permits the use of sesame oil in India, the African, Eastern, and North American colonies, in the preparation of the official liniments, oint-

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\* Read and demonstrated with specimens before the meeting of the N. Y. State Pharmaceutical Association, June 21, 1910, at Saratoga Springs.

ments, and plasters for which the British Pharmacopœia orders that olive oil should be used.

Sesame oil has the following advantages over cottonseed and olive oil:

1. It does not readily turn rancid.
2. It is easily saponified even by cold process.
3. It is a semi-drying oil.
4. It is not gummy and sticky.
5. It is more readily absorbed by the skin.
6. It is thinner than cottonseed oil although of the same specific gravity, in other words it possesses less viscosity.
7. It does not congeal until  $-5^{\circ}$  C. and solid particles do not separate until  $-3^{\circ}$  C., while cottonseed oil congeals at  $0^{\circ}$  C. and solid particles separate already at  $+12^{\circ}$  C., and olive oil congeals at  $0^{\circ}$  C. and solid particles do not separate at  $+10^{\circ}$  C. For the latter reason sesame oil is much to be preferred in colder climates.
8. Its price is reasonable, \$1.00 or less per gallon according to quantities.
9. Its price is not apt to market fluctuation as, owing to the *extensive cultivation*, the *rapid growth* of the plant, and the *double annual harvest* of the seed, a very large quantity of sesame oil is produced.

#### OLEUM SESAMI DELETED FROM THE U.S.P. VIII.

The leaves of sesame were official in the U.S.P. 1830 (1st revis.) to U.S.P. 1880 (6th revis.) inclusive. Sesame oil was official in the U.S.P. 1830 to U.S.P. 1890 (7th revis.) inclusive. Unfortunately, however, it was not admitted again into the U.S.P. VIII. I am informed by a member of the former Revision Committee that the step was taken because the general opinion of the majority of the members was that sesame oil was antiquated and was no longer in use.

Those interested in pharmaceutical history, and I hope their number is on the increase, will undoubtedly be pleased to hear that oleum sesami is a very old if not *the oldest* oil known. Herodotus (born 484 B. C.), the father of history, states that it was the best known oil at that time. According to G. P. Forrester in the *Chemist and Druggist*, London (abstracted in the *American Druggist*, June 13, 1910, p. 308), the word sesame occurs in an Egyptian document of about 1500 B. C.

Any of you further interested in the history of sesamum I would recommend to look up the masterwork of the German pharmaceutical historian, Dr. Hermann Schelenz, "Geschichte der Pharmazie."

OLEUM SESAMI SHOULD BE ADMITTED INTO THE U.S.P. IX.

I can, however, not agree with the decision of the old Revision Committee that sesame oil is antiquated and no longer in use. It has been official right along in a number of pharmacopœias, it has been used officially and unofficially in the preparations of a large number of galenicals and it has been admitted to all the recent pharmacopœias. As I said before the British Pharmacopœia sanctions the use of oil of sesamum in place of olive oil in the British Colonies. Inasmuch as the revisers of the foreign pharmacopœias are convinced of the value of this oil and in view of the many experiments, for a period of several years, which I and other pharmacists have made with oil of sesamum in various galenical preparations, I sincerely hope that the present Revision Committee will consider the admission of this oil into the new U.S.P. and its use in several galenicals.

EXPERIMENTS WITH OLEUM SESAMI.

The use of sesame oil by the writer dates back about 20 years, when he prepared a hair oil or macassar oil, colored red with alkanet and suitably perfumed, which in those days had a very large sale, undoubtedly due to the fact that it was less oily, less sticky and gummy, and more readily absorbed and penetrating than others. Oil of sesamum has been used for anointing in ancient times and is mentioned as such in the Bible and is described for this and other uses by Dioscorides, that most important author, whose works on pharmacology and the entire materia medica were authoritative down to the sixteenth century. Xenophon, the last of the three great Greek historians, writes in his *Anabasis* or *Expedition of Cyrus* (371 B.C.), an account of "the retreat of the ten thousand," a part of the army of Cyrus, after the unfortunate battle of Kunara, that by the application of sesame oil they prevented their hands and feet from becoming frostbitten.

The following are a few of the external preparations with



which I have experimented for a number of years. Specimens are herewith submitted and some of the galenicals will be prepared before you extemporaneously.

LINIMENTUM AMMONIÆ.

Undoubtedly all of you are familiar with the shortcomings of the present U.S.P. formula for this liniment, which are: 1. Four ingredients instead of two. 2. The cumbersome method. 3. The yellow color. 4. The separation into layers. 5. The thinness when freshly prepared. 6. The thickening by age.

It is certainly impracticable to mix four ingredients together when five cents' worth of hartshorn liniment is called for, the U.S.P. stating: "The liniment should be freshly prepared when wanted."

Although Eugene Dieterich, the great German manufacturing pharmacist, is generally credited with the original use of sesame oil in the preparation of ammonia liniment, I have found that as early as 1884, F. M. Alcock states on page 282 of the *Pharmaceutical Journal and Transactions*, London: "Sesame oil makes a more satisfactory ammonia liniment than olive or other oils;—even after standing three (3) months there is no sign of separation and the liniment presents a beautiful creamy consistency and color but slightly altered during the time stated."

From experiments during a period of several years I have arrived at the conclusion that as per demonstration you can prepare an ideal ammonia liniment by shaking together: sesame oil, 3 parts by weight, and ammonia water, 1 part by weight.

My opinion is that it is an advantage, being easier and cleaner, to weigh the ingredients instead of measuring them.

This liniment has the following advantages:

1. It contains only 2 ingredients.
2. It can be prepared quickly and easily.
3. The resulting liniment is snow-white.
4. It is homogeneous and does not separate into two layers.
5. It has the proper creamy consistency, not too thick and not too thin.
6. It is permanent and will not thicken materially by age, as you can convince yourself by a specimen over a year old.

## LINIMENTUM CALCIS.

Although the U.S.P. formula for lime liniment or carron oil, *i.e.*, equal volumes of linseed oil and lime water, is perfectly satisfactory, I wish to call your attention to the liniment prepared with oleum sesami which is official in the Japanese Pharmacopœia III, 1905. As you see by this extemporaneous preparation equal parts, by weight, of sesame oil and lime water will give at once a beautiful, white, homogeneous liniment.

## LINIMENTUM CAMPHORÆ.

The employment of heat in the present U.S.P. directions has unquestionably been the direct cause of court decisions that the preparation *cannot* contain 20 per cent. of camphor.

Sesame oil is much to be preferred to cottonseed oil: first, because it is not gummy or sticky; second, because it is readily absorbed by the skin; and third, because it is a better solvent for camphor as the same dissolves easily without the aid of heat.

Circulatory displacement, without heat, in my experience is *the* ideal method of preparing a full-strength camphorated oil, which synonym will undoubtedly be admitted in the next revision.

Our U.S.P. should include besides a short physical description including specific gravity also an assay for determining the strength of camphor liniment. The Austrian Pharmacopœia VIII, 1906, which orders one part of camphor and three parts of oleum sesami, gives the following approximate method for determining the strength: When 10 c.c. of oleum camphoratum and alcohol are well shaken together in a graduated tube, then the separated alcoholic layer should not measure less than 13 c.c. While this is not an exact assay, it will certainly serve as an approximate test which can be easily applied by the average pharmacist. Experiments in the application of this test to the U.S.P. camphor liniment are going on in my laboratory and will be published in due time.

## INFUSED OILS.

*Infused oils* and quite especially *Oleum Hyoscyami Infusum* N.F. or, as it is named by the foreign pharmacopœias, "*coctum*." The process employed in the N.F., as well as the foreign pharmacopœias, is the Eugene Dieterich method, consisting of macerating

the ground drug with ammoniated alcohol to liberate the alkaloids and then infusing with the oil. Olive oil was formerly used, but sesame oil has replaced it in the newer pharmacopœias and sesame oil should most certainly displace the poor mixture of lard and cottonseed oil in the N.F. When the fourth edition of the Swiss Pharmacopœia was published, I discovered that this authority describes this oil as "dark green and clear," and orders its preparation in a copper vessel. As you can convince yourselves from submitted specimens, an oil results with a beautiful rich dark green color. In place of a copper vessel any ordinary dish will answer if a few copper coins are added when the oil is infused.

Although color is said to be no criterion in pharmacy, I am fully convinced that the physician as well as the patient and customer will prefer such a beautiful preparation to one of a brownish-green or greenish-brown color. The psychological effects alone of such an elegant galenical will benefit the patient.

Last, permit me to direct your attention to the use of sesame oil in place of olive oil in the U.S.P. and N.F. Oleates, and quite especially if they are intended to be absorbed.

#### CONCLUSION AND SUGGESTIONS.

In conclusion I want to emphasize the fact that I have no commercial interests whatsoever in sesame oil. The reason that I am so much in favor of this oil is that through years of experiment I am fully convinced from the practical as well as the scientific point of view that *oleum sesami* deserves admission into galenical preparations of the U.S.P. IX and N.F. IV.

I sincerely hope that in the resulting discussion a great many valuable points will be brought out and also that some of the members of the N. Y. State Pharmaceutical Association will give sesame oil a trial, report their experiments, and thereby be helpful to the U.S.P. and N.F. Revision Committee.

## PROGRESS IN PHARMACY.

By M. I. WILBERT, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

(Concluded from page 450.)

BUCHU.—E. M. Holmes reports a new adulterant of buchu which he has recognized as the leaflets of *Psoralea obliqua*, E. Mey, a small shrubby plant, 2 to 4 feet high, common near Stellenbosch, about 25 miles east of Cape Town, and therefore in the district where *Barosma betulina* grows (*Pharm. J.*, London, 1910, p. 69).

CACTINA AND CACTIN.—E. P. Lyon and Guy L. Qualls report a series of experiments and observations on the influence of these substances on animals and on the pulse-rate and blood pressure in man. No effects were discoverable from the use of either cactin or cactina.

An editorial in calling attention to the report points out that the lavishness with which the two substances are being advertised would appear to indicate that they are still widely used and concludes that as a central theme for a treatise on the "Psychology of Advertising" these products may have their uses, they certainly illustrate the credulity of many otherwise well balanced medical men (*J. Am. M. Ass.*, 1910, v. 55, pp. 455-459 and 508).

DIGITALIS.—An editorial commenting on the proposed Government supervision of the standardization of digitalis, as suggested by Schmiedeberg, points out that this recommendation would virtually take the drug beyond the control of pharmacists, and questions the advisability of having a Government department acting as custodian of the drug (*Chem. and Drug.*, Lond., June 18, 1910, v. 76, p. 50).

NEW DIGITALIS PREPARATION.—A patent, issued to Tambach and Knoll, provides for the making of a preparation of digitalis which is to embody all of the activities of the fresh drug. The preparation is made by treating an alcoholic extract of the drug with ether, removing the resulting precipitate, concentrating the filtrate, and mixing the residue with milk sugar (*Pharm. Post*, Wien, 1910, v. 43, p. 502).



ERGOT.—Gordon Sharp presents an interesting historical study of ergot, its origin, botany, and chemistry. Under the latter heading he reviews, at some length, the more recent work on the chemistry of ergot and concludes with a review of the toxicology, pharmacology and therapeutics of the drug (*Pharm. J.*, Lond., 1910, v. 85, pp. 38 and 68).

Barger and Dale report the isolation of an active principle from ergot extracts which they believe to be the substance responsible for the intense activity exhibited by some ergot extracts in producing contraction of the isolated uterus of the cat. The relative abundance of this principle in dialysed extracts suggested that it was wholly or partly produced by micro-organisms and this supposition was confirmed by physiological experiments (*Pharm. J.*, London, 1910, v. 30, p. 757).

METHYL ALCOHOL.—George Arends believes it would be justifiable to investigate further the possibility of using purified methyl alcohol as a solvent for pharmaceutical preparations that are to be used externally. While he admits that the available literature is strongly against the use of this solvent at the present time, he appears to feel that much of the available evidence is misleading and that the reported deleterious results may be due entirely to the contaminating materials found in the commercial wood alcohol (*Pharm. Ztg.*, 1910, v. 55, p. 588).

The above suggestion has been vigorously opposed in Germany as being fraught with possible danger and it has been pointed out that the bulk of the available evidence would appear to indicate that even chemically pure methyl alcohol is dangerous. Until this evidence has been shown to be fallacious it would, of course, be inadmissible to use methyl alcohol as a solvent in any medicinal preparation.

MEXICAN JALAP ROOT.—E. M. Holmes points out that the French, German, Danish, and United States Pharmacopœias each requires that jalap yield 7 per cent. of resin, while the Belgian and Dutch Pharmacopœias require 8 per cent. He asserts that recently jalap assaying as high as 17 per cent. of resin has appeared on the London and Hamburg markets and attributes the improved quality to the unusually high price. He maintains that a good market price is almost certain to lead to a supply of good quality and that a price that will not pay the collector will depreciate the quality of any drug (*Pharm. J.*, London, 1910, v. 30, p. 789).

NUCLEIN, NUCLEIC ACIDS, AND NUCLEATES.—A general article describing these compounds has been prepared by the Council on Pharmacy and Chemistry for publication in N.N.R.

These products have been more or less widely used but their true value is as yet undetermined and many capable observers are inclined to think that the claims that have been made for the therapeutic value of these compounds are not based on sound conclusions (*J. Am. M. Ass.*, 1910, v. 55, p. 503).

OIL OF ROSE.—An editorial asserts that this year an unusual variety of adulterants have been put in the stills in the manufacture of otto of rose in Bulgaria and cautions the buyers to be on their guard (*Chem. and Drug.*, London, July 30, 1910, p. 149).

PODOPHYLLUM RESIN adulterated with aloes is reported by Joseph H. Williams who found approximately 25 per cent. of powdered aloes in a sample of resin of podophyllum which came within the limits of the tests prescribed by the Ph. Brit. IV. Williams thinks it would be advisable to apply tests for water soluble material in resin of podophyllum (*Pharm. J.*, London, 1910, v. 30, p. 608).

PUMPKIN SEED AS A VERMIFUGE.—H. H. Dale reports a pharmacologic study of pumpkin seed. He finds that neither the expressed oil nor the resin exert any anthelmintic or other physiological action. He holds that any value that the seeds may possess when administered in substance must be attributed solely to mechanical action.

In a further contribution Power and Salway report that they have failed to find any alkaloid, glucoside, or other definite compound likely to possess therapeutic action (*Pharm. J.*, London, 1910, v. 30, p. 703).

QUININE AND UREA HYDROCHLORIDE is being used quite widely as a local anæsthetic. In a recent number of the *Journal of the American Medical Association* (June 11, p. 1940), W. O. Green reports 4 cases in which the substance was used with apparently satisfactory results.

QUININE ARSENATE.—The Council on Pharmacy and Chemistry of the American Medical Association reports that quinine arsenate was submitted to the staff of clinical consultants and, on their recommendation, refused recognition in New and Non-official Remedies because it does not appear that this preparation possesses any properties that may not be found in a simple mixture of its components. Attempts to substitute it for other quinine salts would

lead to overdosing with arsenic (*J. Am. M. Ass.*, 1910, v. 55, p. 235).

SCOPARIUS.—J. Chevalier reports a systematic study of the sparteine content of scoparius at different seasons of the year. For the whole plant the highest, 0.68 per cent., was found in March. This rapidly decreases, being but 0.325 per cent. in April. The minimum is reached in August, 0.233 per cent., and from this a gradual rise to November with 0.475 per cent. The dried and ripe fruit was found to have 1.10 per cent. of sparteine (*Apotheker Ztg.*, 1910, v. 25, p. 466).

SCOPOLAMINE.—Delbet and Dupont warn against the use of scopolamine for general anæsthesia; their review of 120 cases includes 2 fatalities, one serious post-operative syncope, and a number of other mishaps (*J. Am. M. Ass.*, 1910, v. 55, p. 257).

SPRITOL is the name given to a substitute for ethyl alcohol that on examination was found to consist of wood alcohol (*Apoth. Ztg.*, Berlin, 1910, v. 25, p. 136).

VIROID.—Dr. Henry Freeman Walker suggests the word "Viroid" as a generic term for designating the biologic specifics used in active immunization. He believes that this name would be distinctive in that it would indicate, with the necessary prefix, the virus for which it would be used as an antidote. It would also restrict "Vaccine" to the now well-established cow-pox virus (*J. Am. M. Ass.*, 1910, v. 55, p. 42).

DRUGS.—J. Biberfeld (*Deut. Med. Wchnschr.*), in a review of the pharmaceutical harvest of the last few years, asserts that not much grain is left after separating it from the chaff (*J. Am. M. Ass.*, 1910, v. 55, p. 541).

AN ALKALOIDAL SYNTHESIS.—Pictet and Finkelstein ("Berichte," xlii, 1979) have succeeded in synthesizing the alkaloid laudanosine (methyl-tetra-hydro-papaverine) by the interaction of homoveratrylamine and homoveratric acid. The latter body is prepared from eugenol by the method elaborated by Tiemann and Matsmoto (*Chem. and Drug.*, London, July 30, 1910, p. 159).

FLUIDEXTRACTS.—An interesting and timely contribution to the preparation and valuation of galenical preparations is presented by the chief apothecary of the city hospital, Berlin, H. Linke.

He reviews the introduction of fluidextracts in the German Pharmacopœia, the expectations that were expressed twenty years ago, and the failure of these expectations to materialize on account

of the difficulties involved in the production of these preparations.

In common with other observers he notes that the complete exhaustion of a drug requires from 5 to 8 times the weight of the drug itself. He also discusses the economic questions that are involved in the production of fluidextracts by manufacturers, the variation in the price of the preparations, and presents a table giving the results of his observations on a number of commercial preparations and an equal number made in the laboratory of the hospital with which he is connected (*Apoth. Ztg.*, Berlin, 1910, v. 25, pp. 522-523).

MELTING POINT DETERMINATION.—L. Derlin recommends the metallic bath as being the most satisfactory for determining the melting point of most organic chemicals used in pharmacy. For substances that melt at higher temperatures the figures are usually low (*Apotheker Ztg.*, 1910, v. 25, p. 435).

Richter Ernst, in discussing the value of melting point determinations, points out the advantage of the apparatus figured in "*Vierteljahresschrift für praktische Pharmazie*, 1907, p. 145. This apparatus has the advantage that the sulphuric acid circulates and heats evenly so that the apparatus can be allowed to stand without further care. To prevent the destruction of the cork he recommends coating it with collodion (*Apotheker Ztg.*, 1910, v. 25, p. 476).

REFRACTOMETER.—The *Chemist and Druggist*, July 16, 1910, p. 51, points out that the next edition of the British Pharmacopœia will probably provide refractive indices for oils and other liquids the quality of which may be determined by examination with the refractometer, an instrument whose value in the examination of essential oils is well established. The article includes a description and illustration of the refractometer generally used.

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## ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITÄT BERLIN.

Of the large number of papers appearing in the annual publication of the work done at the Pharmaceutical Institute of the University of Berlin, none are so important and of such practical value as those which reveal to physicians and pharmacists the false and misleading claims, to say nothing of downright sophistication, made in the



manner of introducing and exploiting many of the so-called newer remedies.

This work of investigation done by the Institute is in line with the effort made by the American Medical Association and so fruitfully carried out by its Council on Pharmacy and Chemistry to inform the physicians of this country how they have so successfully been preyed upon and used by unscrupulous manufacturers.

When one reads of such conditions in other countries, it is apparent that credulity and gullibility are not confined to these United States. It must be exceedingly gratifying to those who are hopeful of better things that there are some men who are both able and willing to do the painstaking analytical work required to determine the truth about remedies intended for the sick, and tell the truth about them without fear or favor. It is only by the greatest possible publicity, in this as other lines of work, that those who desire to profit "by ways that are dark and devious," can be restrained and curbed and made to be honest.

The following abstracts were prepared from the annual publication edited by Dr. K. Thoms, Director of the Institute.

*An Adulterated Acetylparamidosalol.*—In the Pharmacopœia Helvetica IV, acetylparamido phenolum salicylicum is the scientific name for salophen. A careful examination by Zernik, of the contents of an original package labelled acetparamidosalol showed it to be a mixture of 75 parts of the original and 25 parts of acetanilid.

*Eulatin.*—A white, odorless, slightly sour-tasting powder, which the manufacturers claim to be a true chemical compound and termed by them amidobrombenzoic acid dimethylphenylpyrazolon.

Friedmann, in the *Med. Klinik*, 1908, states that it is of use in whooping-cough, that it promotes expectoration, and diminishes the frequency and intensity of the spasm in this disease.

Zernik gives in detail his analysis of the contents of an original package bought on the open market. He found it to be a white, crystalline powder of a bitter taste, slightly soluble in water and completely soluble in alcohol, particularly on warming. The solution gave an acid reaction and a clear violet fluorescence. At 75° eulatin began to liquefy and at 150° it had completely melted. On crystallizing some of the preparation from alcohol, a needle-shaped crystalline body with a constant melting point of 251°–252° was obtained. This behavior signified to him that eulatin must be a

mixture and this assumption was confirmed by the following experiments.

Five-tenths of a gramme of eulatin was mixed three times with 10 c.c. of cold water and after standing a short time the combined solutions were filtered. In the faintly violet fluorescent solution antipyrine was demonstrated in the usual manner; on the other hand, the undissolved residue contained no antipyrine, but showed a melting point of  $251^{\circ}$ .

Five-tenths of a gramme of eulatin was treated in a like manner three times with 10 c.c. cold benzol; the undissolved residue was free of antipyrine and melted at  $251^{\circ}$ .

It, therefore, became necessary to identify this substance with the melting point of  $251^{\circ}$ . Literature contains not less than six isomers of amidobrombenzoic acid, the highest melting point being  $225^{\circ}$ . The foregoing substance proved to be soluble in and lost its acidity in sodium carbonate solution. Several grammes of finely powdered eulatin were shaken in a separatory funnel with a mixture of chloroform and sodium carbonate solution until completely dissolved. The lower chloroformic layer was drawn off and the alkaline solution shaken out twice again with chloroform. The combined chloroformic solutions, on evaporation, left a residue of pure antipyrine, melting point  $109^{\circ}$ – $111^{\circ}$ . The alkaline solution was treated with dilute  $H_2SO_4$  to liberate the acid, which was recrystallized from toluol; melting point  $251^{\circ}$ – $252^{\circ}$ .

The crystallized substance gave a negative result with Lasaigne's reagent, showing the absence of nitrogen and therefore of amidobrombenzoic acid, although bromine was found in the substance. A determination for bromine, by the method of Carius, of 0.2690 Gm. of the substance, gave the following result, 0.2520 Gm.  $AgBr = 39.87$  per cent. Br.

Literature records a brombenzoic acid with a melting point of  $251^{\circ}$  known as p-brombenzoic acid.

A mixture of the acid obtained from eulatin and pure p-brombenzoic acid showed a melting point of  $251^{\circ}$ . Besides p-brombenzoic acid eulatin contained still another acid.

On shaking the acid filtrate from the p-brombenzoic acid with ether, a nitrogen body (but free from bromine), acid-like in character, was extracted. It had a melting point of  $144^{\circ}$ – $145^{\circ}$  and proved to be o-amidobenzoic acid (anthranilic acid). A mixture of this with pure o-amidobenzoic acid showed no difference in melting point.

Zernik claims that p-brombenzoic acid is only a mechanically mixed ingredient in eulatin, and that it is hard to believe that o-amidobenzoic acid is chemically bound to the antipyrine. At least the following experiment is evidence against it. If eulatin is extracted with cold, absolute ether, p-brombenzoic acid, o-amidobenzoic acid, and antipyrine go into solution. If the ethereal solution is shaken out with cold water the antipyrine is obtained, while the acids remain in solution in the ether.

It was further ascertained that when eulatin is subjected to a temperature of 100° it loses by weight 0.56 per cent., and when shaken out with chloroform 50.94 per cent. antipyrine is separated.

As a result of his calculations he states that it is a mixture of two parts of p-brombenzoic acid and antipyrine in molecular proportions and one part o-amidobenzoic acid and antipyrine, also in molecular proportions. He says that it is impossible to determine by analytical means just how this mixture is brought about. The declaration that eulatin is "amidobrombenzoësaures antipyrine" he states to be untrue according to his investigation.

Physicians should be very careful, he advises, in accepting recommendations and testimonials of the many preparations of supposedly newer composition on the market.

*Meligrin.*—The makers of this product give no information as to its true nature. A microscopical and chemical investigation by Zernik of the contents of an original package bought on the open market showed it to be a mixture of 86 parts of antipyrine and 14 parts of methylacetanilid (exaligin).

It is a white crystalline powder, very soluble in water, with the bitter taste characteristic of antipyrine.

The manufacturers of this remedy have taken advantage of the fact that antipyrine (like sodium salicylate, chloral, etc.) increases the solubility in water of many organic substances.

*Mergandol* is the name given to a liquid preparation recommended for intramuscular injection for the treatment of syphilis and also for external application on the skin eruptions of the same disease.

The manufacturers state that it is a solution of hydrargyrum-natriumglyceratum in glycerin, each cubic centimetre containing 0.0035 pure mercury.

Zernik says that while sodium glycerate is mentioned in chemical literature, mercury or mercury-sodium glycerate is unknown.

An examination of an original bottle showed it to be a colorless, syrupy liquid of a neutral reaction, specific gravity 1.2177 at 15°. A qualitative analysis showed the presence of glycerin, mercury, sodium, and chlorine. Further quantitative determinations showed that in 100 c.c. of the liquid there were present 0.4944 per cent. of mercuric chloride and 0.9269 per cent. of sodium chloride.

It is conclusively proven by Zernik that mergandol is a solution of these two salts in glycerin and water and not a solution of quick-silver-natrium-glycerates in glycerin.

*Phagocytin*.—Under this name there has appeared on the German market a sterile solution, recommended by the exploiters for subcutaneous injection in septic and exhausting diseases. It is dispensed in ampouls each containing, so the label stated, one cubic centimetre of a 5 per cent. solution of, what the makers claim, sodium nucleinate.

At the request of the Deutschen Apothekervereins the Pharmaceutical Institute undertook an investigation of this preparation.

It was marketed in cartons of twenty ampouls each. The ampouls contained a brownish liquid of an alkaline reaction; upon the addition of a mineral acid a white, flocculent precipitate was formed.

Each ampoul contained somewhat more liquid than the quantity stated on the label.

Upon evaporation of one cubic centimetre of the liquid there remained a brown, amorphous residue which, after drying at 100°, weighed 0.054 gramme, somewhat more than stated on the label.

On heating the residue to ash there developed the characteristic odor of garlic, which led the analyst to suspect the presence of arsenic: this suspicion was later confirmed by positive results with Marsh's and Bettendorf's tests.

In the original solution the presence of arsenic could not be demonstrated in the usual manner. Only after destruction of the organic substance was its presence confirmed by the above tests; it was also precipitated as sulphide with hydrogen sulphide.

The ash of phagocytin showed further the presence of sodium, besides traces of potassium and iron, combined with carbonic, phosphoric, and sulphuric acid.

Further quantitative determinations showed that phagocytin was a 5 per cent. solution of an organic combination of arsenic.

*Plejäpyrin*.—The introducers of this remedy speak of it as being



a very soluble and ideal migraine powder of true chemical combination obtained by the condensation of molecular portions of benzamid and phenyldimethylpyrazolon. They also claim that it can be administered in one gramme doses several times a day, is well borne, and without any untoward after-effects.

A chemical and microscopical examination of an original package of the powder showed it to be merely a mechanical mixture of antipyrine and benzamid. This was later confirmed by mixing antipyrine and benzamid in molecular proportions and subjecting the mixture to the same method of analysis as applied to the original. The results were absolutely the same.

Plejapyrin has been withdrawn from the market.

*Pyrenol*.—In the *Apotheker-Zeitung*, Number 100, 1907, Zernik publishes the result of his analysis of the above-named preparation, and states positively that instead of being a definite chemical compound, as claimed by the manufacturers, it is simply a mixture of well-known chemicals. He also states that the constitutional formula given by the maker is scientifically impossible.

The manufacturer, in a written communication to the Institute, takes exception to Zernik's findings and reiterates that pyrenol is not a mechanical mixture but a true chemical combination which he terms "benzoësäurethymolester benzoyl-oxybenzoësäure neutralized with sodium."

At the request of Dr. Thoms, Professor Gadamer, director of the Pharmaceutical Institute of the University of Breslau, had his assistant Dr. Gaebel undertake and carry out a series of experiments and complete analysis of an original package of pyrenol.

Dr. Gaebel gives in detail each step of his investigation, and concludes by stating that pyrenol is a mechanical mixture of equal parts of sodium salicylate and sodium benzoate with 1 per cent. of benzoic acid and not more than 0.3 per cent. of thymol.

This result practically confirms Zernik's investigation and was in turn confirmed by an exhaustive analysis made by Dr. Thoms himself.

JOHN K. THUM.

## CORRESPONDENCE.

EDITOR AMERICAN JOURNAL OF PHARMACY.

Dear Sir: Your attention is called to the action of the Indiana Board of Pharmacy with a view to its publication in the interests of pharmaceutical education.

The influence of the syllabus is apparent and its bringing of the schools and the boards together is not one of the least of its purposes.

The criticism that the amount of work should require more than 1000 hours is one that is uniformly made by those that give close consideration to the subject, but the facts should be recalled that the campaign for even 1000 hours was long and arduous and that many have not fully recovered from the effects of this standard.

"The Indiana Board of Pharmacy at its meeting on the 14th of this month (July) called a conference of all the schools of pharmacy in the State, each of which sent a representative. After a lengthy discussion the schools with the Board of Pharmacy adopted the syllabus as the standard.

"The criticism of all was that the standard was rather low and that the amount of work should require more than 1000 hours."

The Regents on the recommendation of the New York State Board of Pharmacy advanced the requirements in New York State to 1100 hours, 500 recitations and 600 laboratory.

Handbook No. 11 entitled Pharmacy has just been printed by the Department and copies may be secured without expense on application to the Education Department, Albany, N. Y. It contains the new law, the rules of the Board, notes on the law, the schools registered by the Regents or accredited by the Department, and the synopsis showing the statutory requirements for the practice of pharmacy throughout the United States.

Chairman Engstrom of the Chemistry Branch of the Syllabus Committee has addressed a letter to his subcommittee for suggestions of improvement.

He calls attention to the incomplete character of the work and the criticisms that have reached him.

The pharmaceutical press will confer a favor on the Executive Committee by calling attention to any suggestions, corrections, or discussions that appear in its columns. The letter head gives the names and addresses of the members of the Executive Committee.

Respectfully yours,

H. L. TAYLOR.

ALBANY, N. Y., August 1, 1910.

# BOOK REVIEWS.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. Vol. III. Fourth Edition, entirely rewritten. Edited by W. A. Davis and Samuel S. Sadtler. Philadelphia, P. Blakiston's Son and Co., 1012 Walnut St., 1910. \$5.00 net.

In this volume a number of subjects are considered, each having been prepared by special contributors. The chapter on "Hydrocarbons" was written by F. C. Garrett, of New Castle-upon-Tyne, England. The parts on "Bitumens," "Phenols," and "Anthracene and its Associates" were prepared by S. S. Sadtler, of Philadelphia. The monographs on "Naphthalene and its Derivatives" and "Phthalic Acid and the Phthaleins" were written by W. A. Davis, of London. The chapter on "Aromatic Acids" is the work of Edward Horton, of London. "Gallic Acid and its Allies" received the special attention of W. P. Dreaper, of London, and the monograph on "Modern Explosives" was written by A. Marshall, of Naini Tal, India.

While all of the volumes of "Allen's Commercial Organic Analysis" are of interest and value, this one will be of particular interest to pharmacists, as it treats of so many of the compounds that are used either directly or indirectly in medicine. The information given concerning cresols, creosote, creosote oils, phenol, benzoic acid, cinnamic acid and its derivatives, aromatic balsams, cinnamic balsams, salicylic acid and its allies, etc., is extremely valuable. The good features which were noted in the review of Volumes I and II (this JOURNAL, August, p. 381) apply with equal force to Volume III. Finally, it should be noted that in the editorial work of this volume Mr. Sadtler has been associated with Mr. Davis. Professor Leffmann having found it impossible to continue as American editor of the series and at the same time prepare those articles for which he has become responsible, his editorial work will in the future be assumed by Mr. Sadtler.

A TEXT BOOK OF ORGANIC CHEMISTRY. By Prof. William A. Noyes, University of Illinois. Second Edition, Revised. New York: Henry Holt and Company, 1910.

This is one of the best elementary books on "organic chemistry" that has been published. The present edition will be of special interest to pharmacists and physicians, as the chapter on

"Compounds of Interest in Physiology and Pathology" has been rewritten on the basis of the classification of proteins, recently adopted by the American Society of Biological Chemists and the American Physiological Society. A number of other changes and additions have been made.

NORMAL HISTOLOGY, with Special Reference to the Structure of the Human Body. By Prof. George A. Piersol, University of Pennsylvania. 438 illustrations, many of which are in colors. Eighth Edition (Rewritten). Philadelphia and London: J. B. Lippincott Company.

It is indeed gratifying that the medical student has such an excellent text-book on histology as the one in hand. It is well arranged, well written, and profusely illustrated, not only with histological material showing microscopic details, but in some instances with the macroscopic material, as of the human brain, showing the gross anatomy of this organ and the relation of the different parts to each other.

The book comprises over 400 pages and includes chapters on the cell, the elementary tissues, the blood vascular system, the lymphatic system, mucous membranes and glands, the alimentary canal, the organs of respiration, the urinary organs, the male reproductive organs, the female reproductive organs, the central nervous system, and the sense organs. There is also an excellent chapter on microscopical technic.

Much of the work that is here given should be followed by the pharmacist, who engages in the examination of blood, urinary sediments, and other pathological products, and it would seem advisable if hygiene, as now taught in colleges of pharmacy, could be made an entrance requirement, and the time given to this subject at college replaced with some work on the normal histology of the human body.

THE NEW STANDARD FORMULARY. Comprising in Part I all preparations official or included in the Pharmacopœias, Dispensatories, or Formularies of the world, together with a vast collection from other sources. The parts following embracing Domestic and Veterinary Remedies, Proprietary and Synthetic Remedies, Perfumes and Toilet Articles, Soda and other Beverages, and Domestic Utilities. By A. Emil Hiss and Albert E. Ebert. Chicago: G. P. Engelhard and Company, 1910.



The present volume has been so extensively revised and greatly enlarged that it is more than double the size of the original Standard Formulary. Each primary topic as "Abstracts" has an introductory paragraph which will be found helpful in making those preparations of a given class where formulas may not be given.

The book represents an immense amount of work, not only in collating the information, but in editing, and so far as we have been able to determine has been exceptionally well done. It will be found indispensable to pharmacists and manufacturers.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Revised by W. Harrison Martindale and W. Wynn Westcott. Fourteenth Edition. London: H. T. Lewis, 136 Garver St., W. C., 1910.

Owing to the introduction of a large amount of new matter the form of the "Extra Pharmacopœia" has been slightly changed, the size of the page of the present volume being  $6\frac{5}{8} \times 4\frac{1}{2}$  inches. There are new chapters upon *Acidi Lactici Bacilli*, Organic Arsenic Compounds, Iontaphoresis, Radium, etc. About 100 additional patent and proprietary medicines are described.

In a special volume forming an Addendum to the "Extra Pharmacopœia" is a chart for the recognition of organic chemical bodies used in therapeutics. In this are given facts regarding the solubility, effects of reagents, heat, etc., upon over 300 different substances.

DIGEST OF COMMENTS ON THE PHARMACOPŒIA of the United States of America (Eighth Decennial Revision) and the National Formulary (Third Edition) for the Calendar Year ending December 31, 1907. By Murray G. Motter and Martin I. Wilbert. Washington: Government Printing Office, 1910.

This is the third volume of "Digest of Comments" edited by Dr. Motter and Mr. Wilbert and published under the direction of the Surgeon-General of the Public Health and Marine-Hospital Service of the United States, and constitutes Bulletin No. 63 of the Hygienic Laboratory. It is exceedingly gratifying that these volumes are appearing with the rapidity that they are, as the references are more complete and the abstracts more satisfactory than in any other publication available. The favorable comments which have been made in this JOURNAL regarding the previous Bulletins relating to "Digest of Comments" apply to this volume in hand.

The wisdom of the Board of Trustees of the U. S. Pharmacopœial Convention (1900), in effecting the co-operation of the Surgeon-General of the Public Health and Marine-Hospital Service of the United States in this work, is becoming more and more apparent as each volume of "Digests" appears.

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### THE ORGANIZATION OF ILL-HEALTH.

There are a number of commercial interests in this country that do not want an independent national department of health. In recent years we have had many exposures of the patent medicine swindle. We have learned that most of the most popular patent medicines, the so-called tonics, were nothing more than dilute alcohol with certain bitter drugs so as to make them taste medicinal. Physicians have seen alcohol habits formed as a consequence of freely imbibing these alcoholic preparations. Some of them were meant particularly for women's diseases, and the consequence has been a feminine nipping at alcoholic products that has worked serious harm to the women of the country. We have also found that the headache powders so commonly advertised were composed of drugs which, when taken as freely as was advised on the labels of many of these preparations, were seriously dangerous. We have had not a few, but many, deaths as a consequence of them. The soothing syrups for children mostly contained opium and were seriously injuring the growing child at an important period of its development, and adding to the number of nervous wrecks with tendencies to drug addictions in after life that we had in this country.

For a time after these exposures the patent medicine swindlers were very quiet. In many cases their advertisements disappeared from their usual places. Now they are gaining courage again. The American people have proverbially a very short memory for such exposures. The patent medicine people dread very much the organization of a national department of health, because this will sadly interfere with their now happy prospect of reviving their business and fattening their purses at the cost of the health of our people. This is one element in the opposition organized for ill-health.

There are others. There are a number of people in this country who would like to be freer to foist drugs, impure foods, and ques-

tionable products of many kinds on our inhabitants, so as to make money, cost what it might in the health of those who consumed them. The consumer's purse they are interested in, but not his health. The organization of the national Bureau of Health, with its strict enforcement of the Pure Food and Drugs Act, and its sure tendency to further protect by legislation the health of our people, is a dread spectre to such exploiters of the public, and, of course, they want to lay it if possible.

The League for Medical Freedom has a rallying cry. It is that the doctors are trying to create a medical monopoly—a doctor's trust. They insist that the Owen bill is due to the American Medical Association. As a matter of fact the bill emanates from the Senator from Oklahoma himself, and the movement for a national department of health has been organized, not by the American Medical Association, but by the Committee of One Hundred of the American Association for the Advancement of Science. This organization, as is well known, consists not of physicians, but of the united scientists of the country, and only a very small proportion of physicians are in the membership. The Committee of One Hundred contains the names of many of the representative thinking citizens of this country. They come from all over the country. It is absolutely absurd to talk about such men as organizing a medical trust. Practitioners of all the different cults in medicine are agreed that a national department of health would be a good thing, and cannot possibly interfere with present State laws as to medical practice. This organization of opposition should of itself be a strong argument for the Owen bill. We have the Organization of Ill-Health for commercial reasons. Let us recognize and appreciate at their true value exactly the elements that are engaged in it. —*The Independent*; reprinted from *Science*, July 15, 1910, pp. 84, 85.

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#### PROFESSOR CHARLES F. CHANDLER.

Professor Chandler, who has been the Professor of Chemistry in the College of Pharmacy of the City of New York since 1866, delivered a farewell address to the members of that college on Tuesday evening, March 15, 1910, and at a testimonial dinner tendered to Professor Chandler by the officers, trustees, faculty, and members,

and the Alumni of the college at the Hotel Astor on March 28, 1910, a beautiful silver loving cup was presented to Dr. Chandler and the following resolutions were adopted:

## WHEREAS

CHARLES F. CHANDLER,

A.M., PH.D., M.D., LL.D., D.SC.,

during the forty-three years of his connection with this college, has by his constant earnest work for the increase of its educational facilities contributed in a large degree to its advancement from a small school of pharmacy to a department in Columbia University, and

WHEREAS, As Professor of Chemistry and Professor of Organic Chemistry, he has shown in his lectures a masterly delivery and a wealth of illustration that have commanded the respect and esteem of his classes and made each student a personal and enthusiastic friend; therefore be it

*Resolved*, That we hereby express our high appreciation of his distinguished services to the institution, our regret that he wills at this time to retire from its faculty, with our earnest hope that he may for many years enjoy the love and esteem of his hosts of friends, and the well-earned honors universally conceded to his eminence in the profession to which his life has been devoted. And be it further

*Resolved*, That these resolutions be spread in full upon the college records and a copy suitably engrossed be presented to him.

A testimonial dinner was also tendered Dr. Chandler by his former students and associates of the faculty of Columbia University at the Waldorf-Astoria on April 2, 1910.

The chemists of America, including The Chemists' Club, The Society of Chemical Industry, The American Chemical Society, The American Electro-Chemical Society, The American Institute of Chemical Engineers, and The Verein Deutscher Chemiker tendered Dr. Chandler a banquet at the Waldorf-Astoria on April 30, 1910.

The resignation of Dr. Chandler, after nearly fifty years of efficient and devoted service, has elicited such a spontaneous outburst of appreciation and affection from his former students, colleagues, and fellow-scientists that it was deemed appropriate and desirable that a permanent record should be made of the several banquets tendered to Dr. Chandler by his friends and to enumerate and describe the testimonials presented to him. These are published in a "Testimonial Supplement" of the *Columbia University Quarterly* of June, 1910.







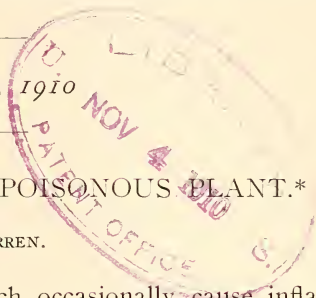
DWARF SUMACH, RHUS MICHAUXII.

# THE AMERICAN JOURNAL OF PHARMACY

NOVEMBER, 1910

## RHUS MICHAUXII—A NON-POISONOUS PLANT.\*

BY L. E. WARREN.



Numerous plants are known which occasionally cause inflammatory conditions when brought in contact with the human skin. While the majority of these are but slightly poisonous to most individuals and some, like the ladyslipper<sup>1</sup> and the Indian pipe,<sup>2</sup> are irritant only to the most sensitive skins there are a few which so generally cause untoward symptoms that they are ordinarily considered venomous. Although representatives of more than forty families of plants have been accredited with poisonous properties of this nature,<sup>3</sup> the most of those commonly designated as poisonous belong to a single order, the Anacardiaceæ (Cashew family). Representatives of this family occur in great numbers in the Tropics and are found less abundantly in all of the temperate regions of the globe. Many genera in the Cashew family contain poisonous species, the genus *Rhus* probably claiming as many as any other.

About 120 species of *Rhus* are known,<sup>4</sup> but of these only about 20 are thought to be poisonous. All of the venomous species contain a viscid, pale cream-colored, emulsion-like juice, which

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\* We are indebted to Prof. William Trelease, Director of the Missouri Botanical Garden, for the use of the electrotpe showing the habit of *Rhus Michauxii*, and which was used to illustrate an article in Volume XX, Report of the Missouri Botanical Garden.—EDITOR.

<sup>1</sup> Babcock, H. H.: *The Pharmacist*, 8, 1 (1875); also A. Ph. A. Proc., 23, 137 (1875). MacDougal, D. T.: *Gard. & For.*, 9, 40 (1896).

<sup>2</sup> Young, A. H.: *Bot. Gaz.*, 3, 37 (1878).

<sup>3</sup> White, J. C.: "Dermatitis Venenata," 29 (1887).

<sup>4</sup> Britton and Brown: *Ill. Flor.*, 2, 386 (1897).

contains the poisonous principle as its chief ingredient. Through an oxidizing process engendered by an enzyme this juice begins to darken at once on exposure to air and eventually becomes converted into a black, lustrous, exceedingly durable varnish which, in Oriental countries, is much esteemed. An alcoholic extract of the juice contains the poisonous principle and gives characteristic precipitates or colorations with alcoholic solutions of certain metallic salts.

In a recent compilation of the poisonous species of *Rhus*<sup>5</sup> by the author it was noted that while further exploration might increase the number already known, additional investigation might eliminate some already classed with the venomous species. The question of the poisonous properties of one of the species, *Rhus Michauxii*, has been under discussion for nearly a century.

*Rhus Michauxii* or dwarf sumac, the smallest and least common of all the sumacs, is a shrub with stout, erect stems from one to three feet in height. It is a rare and little known plant, found only in limited areas in the sandy soils of Georgia and the Carolinas. The deciduous, compound leaves are from 12 to 14 inches in length, with from 7 to 13 lanceolate or ovate, very short stalked, coarsely serrate, pubescent leaflets. The flowers are very small and inconspicuous, growing thickly in a dense panicle which is about 6 inches long by nearly 3 broad. The fruit is a one-seeded, nearly globose drupe, about an eighth of an inch in diameter, clothed with a close pubescence of short, stout, crimson hairs.

*Rhus Michauxii* Sarg. (*R. pumilum* Michx.) [*Schmaltzia Michauxii* (Sarg.) Small] was first described by Andre Michaux,<sup>6</sup> a distinguished French traveler and botanist, who visited this country late in the eighteenth century. While Michaux has left an accurate description of the plant he makes no mention<sup>7</sup> of any venomous properties in connection with it. This omission is significant, since

<sup>5</sup> Warren, L. E.: *Pharm. Jour.*, 83, 531 (1909).

<sup>6</sup> Michaux, A.: *Flor. Bor. Am.*, 1, 182 (1803).

<sup>7</sup> Michaux's work, the "*Flora Boreali Americana*," was not published until after his death. Most of the plant descriptions were written by the editor, Richard, and were based upon specimens collected by Michaux during his travels and supplemented by notes from his journal. Portions of Michaux's journal, edited by Prof. C. S. Sargent, were published (in French) in the proceedings of the American Philosophical Society in 1889. An English translation of this has also appeared (Thwaites: *Early West. Travels*, vol. 3, pp. 1-104, 1904).



Michaux was an accurate observer and was familiar with the Indian traditions and local beliefs of the settlers concerning the floras of the regions which he visited.

The first report of the poisonous properties of *Rhus Michauxii* was made by Pursh,<sup>8</sup> who says (of *R. pumilum*):

"Not above a foot high; it is the most poisonous of the genus, according to information from Mr. J. Lyon, who, by collecting the seed of this species, got poisoned all over his body, and was lamed for a considerable time."

Apparently no other evidence concerning the toxicity of this species was available to Pursh. Thus the unsavory reputation under which *R. Michauxii* has labored for more than ninety-five years was acquired from the testimony of a single observer—an individual who, apparently, was neither a physician nor a botanist.

For many years the statement of Pursh remained unchallenged. There were but few works on systematic botany or catalogues of American plants at that day and still fewer existed which were of sufficient scope to include such rare and little known plants as *Rhus pumilum*.<sup>9</sup>

An examination of the botanical works produced between 1815 and 1870 reveals little concerning *R. pumilum* except the copying of Pursh's assertions, although a few writers deny that the plant is poisonous. The following abstracts and excerpts from the literature of that period illustrate the uncertainty concerning the properties of the plant:

"Reported on the authority of Mr. Lyon to be very poisonous."<sup>10</sup> Rafinesque classes *R. pumilum* with the poisonous species but gives no individual description of it.<sup>11</sup> It is quite probable that he had no personal knowledge of the species for, although he had traveled extensively through the eastern portion of the United States, it does

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<sup>8</sup> Pursh, F.: Flor. Am. Sep., 1, 204 (1814).

<sup>9</sup> In the Journal of Michaux's travels, edited by Prof. C. S. Sargent (Am. Phil. Soc. Proc., 26, 132, 1889), this species is mentioned as "*Rhus pumila*." A specimen was collected or noted by Michaux on April 5, 1796, near Waxsaw Creek in South Carolina. In the "Flora Boreali Americana," the species is called "*Rhus pumilum*." The latter name was most generally accepted by botanists until Sargent renamed the species in 1895 (Gard. & For., 8, 404, 1895).

<sup>10</sup> Elliott, S.: Sk. Bot. S. Car. & Ga., 1, 365 (1821).

<sup>11</sup> Rafinesque, C. S.: Med. Flor., 2, 257 (1830).

not appear <sup>12</sup> that he had visited the Carolinas or was familiar with the flora of that region.

"Fruit clothed with a red, silky pubescence. Said to be very poisonous." <sup>13</sup>

"It is rather rare but occurs in the lower and middle districts, especially in Mecklenburg where it was discovered by the elder Michaux. Pursh has represented it as being very poisonous, but it is perfectly harmless. . . ." <sup>14</sup>

The opinions of later writers concerning the question are not less contradictory than are those of the earlier ones. Millspaugh mentions that there is a great diversity of opinion concerning its toxic or non-toxic effects.

". . . some writers claiming it to be entirely innocuous, others judge it to be the most poisonous of the North American species, claiming that it will show its effects upon those who are not susceptible to the influence of *R. toxicodendron*." <sup>15</sup>

The revival of the theory that the species is poisonous appears to be due to Sargent who reports:

"The juices of *R. Michauxii* turn black in drying, like those of several of the species of *Rhus*. . . . From my limited experience with a partly dried specimen I am inclined to believe that it is the most poisonous of the North American species." <sup>16</sup>

Almost simultaneous with Sargent's publication another authority, Dr. W. W. Ashe, declares with equal emphasis that the plant is innocuous:

"Lyon avers <sup>17</sup> that he was severely poisoned by handling the plant, but it must have been another plant or he was hypersensitive to *Rhus* poisons. Negro children, where *R. pumila* grows, eat its berries with the same avidity as those of *R. Glabra* or *R. copalina* and experience no symptoms of poisoning." <sup>18</sup>

<sup>12</sup> Rafinesque, C. S.: Life and Travels (1836).

<sup>13</sup> Darby, J.: Bot. S. States, Pt. 2, 254-5 (1857).

<sup>14</sup> Curtis, M. A.: Geolog. & Nat. Hist. Surv. N. Car., 3, 15 (1867).

<sup>15</sup> Millspaugh, C. F.: Med. Plants, 1, 36-2 (1892).

<sup>16</sup> Sargent, C. S.: *Gard. & For.*, 8, 404 (1895).

<sup>17</sup> Ashe, W. W.: Geolog. Surv. N. Car., *Bot. Gaz.*, 20, 549 (1895).

<sup>18</sup> This in itself would not be presumptive evidence that the species were not poisonous, since the ripe fruit of *R. vernix* and *R. toxicodendron* are known to be non-poisonous. That the fruit is red and agreeably acid strongly indicates, however, that the plant bearing it is most probably non-toxic, for none of the other red-fruited species is venomous while all of the well-known poisonous species bear white or cream-colored fruits rich in fats but free from acid.

Shortly after this Gray and Robinson<sup>19</sup> reviewed portions of the evidence in the case both *pro* and *con*, but arrived at no conclusions.

From the foregoing it can be seen that the recorded evidence favorable to the theory that *R. Michauxii* is poisonous is meagre and is largely of the "hearsay" variety. A critical examination of the evidence shows that but one authority (Sargent) has added anything from personal observation to strengthen the theory, while two others (Curtis and Ashe) have each declared their opinion to the contrary.

From a study of the botanical literature of *Rhus* species and from an examination of the fruit of several toxic and non-toxic species, the author, several years since, became convinced that *Rhus Michauxii* could not be poisonous. In correspondence with Professor Wm. Trelease, Director of the Missouri Botanical Garden, it was learned that this noted botanist had arrived at the same conclusion. Professor Trelease says:

"Outside of the *Toxicodendron* group, with the aberrant leaf-scars, buds, and fruits, I have always been somewhat suspicious as to the poisonous properties of sumacs (naturally without failing to give heed at least to a current belief in the poisonousness of other species). For this reason, when I began to grow *R. Michauxii*, ten or fifteen years ago, I took occasion to rub its crushed leaves over my hand and I have several times since repeated the trial without ever suffering the least poisoning, although I am moderately susceptible to the poison ivy, and I am consequently inclined to think that this species is poisonous to only very susceptible individuals, if to any one."

In a later communication he writes:

"It is . . . one of the red-fruited sumacs differing almost generically from the white-fruited poisonous species."

In response to an inquiry as to whether the juice of this species darkens on exposure to the atmosphere (as Sargent had stated) he replied:

"The observation now made is that the nearly colorless sap does not darken as the lacquer varnishes do."

In addition to making observations at the request of the author concerning the plant and its visitors, Professor Trelease kindly

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<sup>19</sup> Gray and Robinson: *Syn. Flor. N. Am.*, I, II, 384 (1895-7).

offered to supply specimens of *Rhus Michauxii* from the Missouri Botanical Garden upon which tests could be made. This was done and the material upon which the tests hereinafter described were carried out was obtained from this source. Having been collected by Professor Trelease from an authentic specimen growing in the Missouri Botanical Garden and shipped under his supervision, there can be no question concerning the identity of the material examined. The author herewith extends his most sincere thanks to Professor Trelease for his courtesies in furnishing the material for examination, for reporting his observations upon the living plant, and for revising the botanical description of *Rhus Michauxii* given elsewhere in this paper.

#### EXPERIMENTAL WORK.

The first lot of material was received April 11, 1910. It consisted of the ends of several small branches with the leaf buds about to open. One of the twigs was cut in small pieces and thoroughly crushed by bruising in a mortar. The disintegrated material was then triturated with alcohol for some time and the mixture filtered. A portion of the filtrate gave no black color or precipitate when treated with an alcoholic solution of potassium hydroxide. Another portion of the filtrate was allowed to evaporate spontaneously almost to dryness and a drop of the syrupy residue tested for poisonous properties, according to the method (slightly modified) of Tschirch and Stevens.<sup>20</sup> This consists in thoroughly rubbing a drop of the suspected liquid into the integument of the forearm by means of a glass rod, thus covering a circular area about 1 cm. in diameter. After thirty minutes the part treated is washed with ether, then with alcohol, and lastly with soap and water. If the substance were poisonous the area treated will exhibit a noticeable redness and perhaps slight itching after twenty-four to thirty-six hours. If a negative result be obtained the experiment is repeated with the difference that the test material is allowed to remain upon the arm for from one to two hours. In doubtful cases a third experiment continuing through twenty-four hours should be carried out. When tested by the above method the alcoholic extract from the twigs of *Rhus Michauxii* showed absolutely no poisonous properties.

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<sup>20</sup> Tschirch and Stevens: *Arch. Pharm.*, 243, 504 (1905); also *AM. JOUR. PHARM.*, 78, 63 (1906).



A portion of the residue obtained by evaporation of the alcoholic extract of the twigs was dissolved as completely as possible in a small quantity of petroleum ether, the solution filtered, and the filtrate poured with stirring into a large excess of petroleum ether. After standing twenty-four hours the mixture was filtered, the filtrate allowed to evaporate spontaneously, and a drop of the residue tested upon the arm as above described. These tests also proved negative.

A second portion of material (part of an inflorescence) was received July 19, 1910. A part of this material was subjected to the treatment and tests described above and with the same result—absolutely negative.

While these observations and experiments do not absolutely prove *Rhus Michauxii* to be innocuous, the evidence is most convincing and the author is of the opinion that further investigations (should they be made) will but furnish additional evidence in support of Curtis' contention, made forty years ago, that the species is entirely harmless.

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- Loudon, 1844, Arb. Fruct. Brit., (2) 552.
- Griffith, 1847, Med. Bot., 185. "Many other species of *Rhus* possess the same (poisonous) properties, in a greater or less degree, among which *R. venenatum* and *R. pumilum*, both natives of this country (America), are

- exceedingly active, and have a powerful influence on persons unsusceptible to the action of the *R. toxicodendron*."
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- Draggendorff, 1898, Heilpfl. Völk. Zeit., 400. Many species of *Rhus*, including *R. pumila*, are mentioned.
- Heller, 1900, Cat. N. Am. Pl., 129. *R. Michauxii* is listed.
- Loundsberry, 1901, South. Wild Fl. & Trees, 306. "Famous among them all is *R. Michauxii* which for nearly or quite a hundred years was completely lost to the world of science. It is but a few years ago that it was

rediscovered." Excellent illustrations of a flowering and a fruiting branch are given.

Small, 1903, Flor. So. East. U. S., 729. *Schmaltzia Michauxii* (Sarg.) Small.

" . . . rarely if at all poisonous."

Thwaites, 1904, Ear. West. Trav., (3) 101. *Rhus pumila* mentioned in a translated portion of Michaux's journal. Evidently collected near Waxsaw Creek, in South Carolina.

Warren, 1909, Pharm. Jour. (83) 531. It is noted that some of the species now classed as poisonous may later be proved to be harmless.

Trelease, 1910, Ann. Rep. Mo. Bot. Gard., (20) 11. An excellent illustration is given of *Rhus Michauxii* as growing in the Missouri Botanical Gardens. The illustration is reproduced as a frontispiece to this paper.

LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION.

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## A NOTE ON THE SO-CALLED EMULSION OF SILVER IODIDE.\*

BY JOHN K. THUM, PH.G.

Pharmacist at the German Hospital, Philadelphia.

When the writer first began to experiment with silver iodide with the object in view of obtaining a perfect suspension of this salt in a liquid, he used the yolk of fresh eggs with ideal results; the precipitation of the silver iodide, obtained by the reaction between potassium iodide and silver nitrate, being allowed to take place in the presence of the egg-yolk. By adhering to this method, the greater part of the resulting silver iodide was kept in colloidal solution.

This method of manufacture was discarded though because of the scarcity and expensiveness of eggs at that time, and which condition still obtains at present.

After some further experiment with mucilaginous substances of various kinds, the Mucilage of Irish Moss of the National Formulary was decided upon as being, next to the albumen, the most efficient and satisfactory.

Recently it occurred to the writer that the use of a typical colloid, such as gelatin, would be productive of better results and, accordingly, some experimentation with this substance was carried on.

Aqueous solutions of a good quality of gelatin were made, ranging in strength from 0.1 to 0.5 per cent.; the solution of the gelatin

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\* Nascent Silver Iodide. By M. I. Wilbert, Ph.M., AMERICAN JOURNAL OF PHARMACY, Feb., 1906.

being facilitated by slightly warming. A rather curious thing about the precipitation of the silver iodide, which was obtained by dissolving the potassium iodide in the gelatin solution, and gradually adding the silver nitrate in small quantities, shaking well after each addition, was, that the resulting precipitate fell immediately to the bottom of the flask after agitation of the flask was discontinued. Shaking at frequent intervals during the next twenty-four to thirty-six hours, however, brought nearly the whole quantity of silver iodide into almost perfect suspension. After the lapse of a week, without any shaking of the flask whatever, there was observed at the top of the flask a very slight margin of supernatant liquor.

As stated above this same method of procedure was carried out with 0.1, 0.2, 0.3, 0.4, and 0.5 per cent. aqueous solutions of gelatin. These various mixtures were allowed to stand, protected from light, at room temperature, for a period of at least five weeks, and comparisons made. I might here state that time seems to be an important factor in making these suspensions; from week to week one could notice that they were becoming more and more homogeneous. All of these suspensions of the silver iodide were very good, but to the writer it seemed that the one containing 0.3 per cent. of gelatin was almost perfect. In fact it had the appearance of cows' milk, rich in cream, with but a slight sediment at the bottom of the flask and which was readily suspended by a gentle shaking.

It was not possible to separate this colloidal suspension from the liquid by filtration, because it passed through the pores of the finest filter paper.

Examined under the microscope a drop of the freshly made preparation exhibits the usual appearance of powdered silver iodide. But after the preparation has been made some time a marked change is at once observed. The action of the gelatin, which must be a mechanical one, has reduced the silver iodide to a remarkable degree of pulverization.

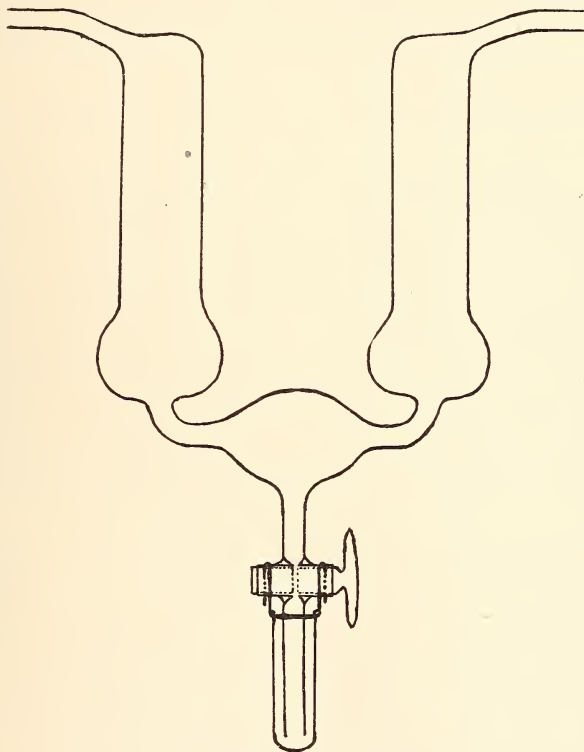


## A MODIFIED DRYING TUBE.

BY EDWIN DOWZARD.

Some time ago the writer was engaged in an investigation which required the use of a train of Pelligot tubes, charged with  $\text{H}_2\text{SO}_4$ , for drying purposes.

As the  $\text{H}_2\text{SO}_4$  had to be changed every few days, it was necessary to disconnect the tubes for recharging.



A modified drying tube (Dowzard).

This proved to be inconvenient, owing to the time required to disconnect and connect a rather complicated apparatus. To obviate this, a stopcock was fused to the lower part of the tube, see sketch.

By means of this stopcock, the  $\text{H}_2\text{SO}_4$  may be removed and fresh acid drawn up into the tube by suction.

If it is desired, the tube may be partly filled with pieces of pumice before fusing on the side tubes.

A small test-tube is suspended under the stopcock by means of a copper wire, to catch any drops of  $\text{H}_2\text{SO}_4$  which may fall.

This piece of apparatus has given great satisfaction, as it allows a change of  $\text{H}_2\text{SO}_4$  without the necessity of disconnection.

ANALYTICAL DEPT., Parke, Davis & Co., Detroit, Mich.

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## EXPERIMENTAL PHARMACOLOGY: AN ESSENTIAL IN THE PHARMACEUTICAL CURRICULUM.\*

BY RUFUS A. LYMAN,

Director of the School of Pharmacy, University of Nebraska.

I have been requested to express my views upon this subject. I make no claims to the title of a pharmacologist. I wish to be known as a physician interested in both medical and pharmaceutical education. I suppose because of the interest I have manifested along these lines, I was asked, a short time ago, to organize a school of pharmacy in the University of Nebraska, where it was felt by both educational and professional men that such an institution was needed in order that the young men and women of our State might receive a more efficient pharmaceutical training. My remarks are inspired by my experience as a student of medicine of ten years ago, and as a practitioner, and a teacher of medical and pharmaceutical students since that time.

In a former paper, I have quoted the following statement made by Professor J. T. Halsey of Tulane University: "A study of the current and past therapeutic literature will, I believe, convince any doubter who possesses sufficient knowledge to enable him to form an intelligent opinion, that there is no branch of medical science, other than therapeutics, wherein medical men display a more culpable and harmful ignorance of essential facts than is the case with pharmacology. Without an exact knowledge of the pharmacological action of some, at least, of our important drugs, a physician must become and remain an empiricist, one shooting in the dark with deadly weapons whose range and power are unknown to

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\* Read before the Section on Education and Legislation of the A. Ph. A., Richmond, Virginia, May, 1910.

him,"—a statement every phase of which every medical man knows to be brimming full of truth.

Many have attempted to explain the cause of the present chaotic condition of pharmacology and therapeutics. Medical men everywhere, and in some cases men prominent in the profession, have attributed it to the fact that the teaching of prescription writing has been neglected in our medical schools. In fact, in recent years more criticism from certain sources has fallen to the lot of this minor course than to the whole of the remainder of the medical curriculum. To a medical pedagogue such criticism is amusing. Even in these days of antipolypharmacy the teaching of the elements of prescription writing is necessary and practice in the same is desirable, but one cannot acquire a knowledge of the physiological action or therapeutic application of drugs through any amount of such teaching and practice.

To appreciate the present state of the medical and pharmaceutical sciences and the ignorance that prevails so largely within the profession, it is necessary to recall a few historical facts. As every one knows, historical medicine began with the Egyptians. We infer, however, that medical practice must have begun with the origin of the human race, coincident with the liability to injury and sickness. In the beginning the cause of disease was probably attributed to the indwelling of evil spirits. One may reasonably infer this from the fact that it was so believed later in historical times and the belief is still prevalent among savage tribes and semicivilized nations. Naturally the original method of treatment consisted of prayers and incantations. The making of noises and the application of fire were used to drive the demons from the afflicted. Material methods of treatment came to be used. By accident it was found that certain chemicals and plants seemed to be of value as means of cure. Curiously enough, the more disgusting and nauseating the substance the greater was believed to be its potency in the treatment of disease. A materia medica was developed of such a disgusting nature that civilized people must revolt against it. This came in the eighteenth century. The time was ripe for homœopathy. It came. The reaction set in. The pendulum swung to the other extreme and the early years of the nineteenth century witnessed a period of nihilism. The great Skoda (1805–1881) was its most ardent advocate. However, it was he who paved the way for the rational study of pharmacology and therapeutics. He introduced the methods of auscultation and

percussion, making it possible to study more accurately the effects of disease and consequently the action of remedies.

In 1817 morphine was isolated by Seitürner. Thus, a definite plant product was substituted for an indefinite crude drug. Animal experimentation was begun and gave rise to modern pharmacology.

In a recent article by Doctor Horatio Wood, Jr., entitled, "The Value and Limitations of Physiological Standardization," he points out the fact that experimental pharmacology is a new science, that the first experimental pharmacologist, in the modern acceptance of the term, is still living and teaching. He discusses the danger of error in the biological test and shows the necessity of its use in the standardization of certain pharmacopœial products and the testing of the efficiency of others. He calls attention especially to the work done upon digitalis and ergot by Americans and Europeans, of the new methods introduced by Doctor Reid Hunt in the study of glandular products, and to the fact that the problems which the pharmacologist is asked to solve at once make a herculean task, surrounded by numerous difficulties.

To one who has studied the subject ever so superficially it is evident the treatment of disease by drugs is to be made rational by introducing into our schools courses in experimental pharmacology. I believe the lack of such training is the greatest defect in our present system of medical education.

A student may be very well trained in the fundamental branches of medicine, such as anatomy, chemistry, physics, physiology, bacteriology, and pathology, he may be skilled in modern methods of physical and clinical diagnosis and still know nothing about the changes induced in the physiology of the normal animal body by the introduction of drugs and much less about their use in diseased conditions. For example, as a medical student I remember the importance that was placed upon strychnine as a therapeutic agent. I was taught that it was a tonic par excellence, that it increased all the functions of the body, that it increased the activity of the heart, that, in large doses, it induced convulsions, that it was useful in diseases of the heart, in certain digestive disturbances, in emaciated conditions, etc., etc. In a like manner I was taught the physiological action and therapeutic application of a hundred other substances. When I was through with it all, it seemed the most unsatisfactory subject in the medical curriculum. If, in the beginning, I had been given a frog and told to inject a certain quantity of strychnine into



the lymph sac and had been instructed to study the symptoms, and with the onset of convulsions had been shown how to do a series of simple operations which show conclusively that the convulsions are due to the action of strychnine upon the spinal cord, and not upon peripheral nerves, motor end plates, or muscles, and more than that, if I had been shown that this action upon the cord was due to its effect on certain elements in the cord and not upon others, I would have realized that strychnine was a body which produced marked and definite physiological changes. Having found that its presence (in some unknown manner) caused symptoms which indicated stimulation at a certain point, I would have been in a position to use strychnine rationally in any diseased condition where it might be desirable to increase the activity of the central nervous system and those functions which are controlled indirectly through it.

I would also have had a hint as to its possible uses in the treatment of depressing poisons and as a synergist to the action of other drugs. Strychnine would then have been a reality to me, a useful tool, something I could have used with satisfaction. That simple experiment would have opened a new field of thought. From various sources, we hear expressions of surprise that physicians prescribe proprietary remedies. There is no occasion for surprise. With the training they have received in our medical schools, and which they still receive in the majority of them, it is a surprise that pharmacopœial preparations are prescribed at all. If a school does not furnish a foundation upon which a superstructure may be built, graduates in medicine must still learn therapeutics from the label of the proprietary medicine bottle. This lack of pharmacological training is manifested on every hand among surgeons and medical practitioners of high standing. This leads to the most absurd mistakes. For example, a short time ago I was asked by one of the leading surgeons of Lincoln to step into his operating room and see one of his patients, "who was not doing very well on the table." I found a man undergoing an operation for a ruptured appendix. The abdomen was full of pus. The patient was in a condition of collapse before the beginning of the operation. The heart beat was just discernible. The attendants had just injected subcutaneously in the axilla 1 quart of physiological salt solution to which 6 drops of adrenalin chloride had been added. They were beginning with the second quart so treated. The surgeon remarked that the heart did not respond to the adrenalin. Of course it did not. The active

constituent was oxidized and rendered inert long before it reached the circulation. The patient died. Again, there is an obstetrician in our city who has no superior in the middle west. I lately discovered that he makes a routine of giving 5 drops of adrenalin chloride per os following labor, to cause uterine contraction and to prevent hemorrhage. Of course it is destroyed before it reaches the blood-vessels of the mucosa. I know of another man who gave cocaine by the mouth and was surprised that he did not get local anæsthesia in the skin. I saw another successful practitioner use strychnine hypodermically, in order to lessen the severity of an epileptic convulsion. Such examples might be quoted *ad infinitum*. Such errors would not occur had these men had pharmacologic training and been able to appreciate the pharmacologic point of view.

One physician, a graduate ten years ago from one of the famous eastern medical schools, now a man well known in our State, and a member of the faculty of the University, tells me whenever he has opportunity, that he does not believe students understand pharmacological experimental work. He is of the opinion that it is beyond them. He maintains that they go through the experiments as a matter of routine. This is not so. The average student is a thinking being, his thoughts only need directing. From his pharmacological experiments and observations he will draw conclusions as to the therapeutic uses which as a rule are surprisingly accurate.

My remarks have been made chiefly with the medical student in mind, but they are just as applicable to the training of the student of pharmacy. As pharmacological methods are elaborated and perfected, they will become more valuable in pharmacopœial standardization. I do not mean that we shall make expert experimental pharmacologists out of our pharmacists. That is not possible, but every pharmacist should understand the general principles of the biological test just as he does the general principles of the chemical tests of the Pharmacopœia. Likewise, experimental toxicology is an important subject to the practical pharmacist. In addition, the study of experimental pharmacology has an obvious educational advantage and must increase the standing of the pharmacist with physicians and with the people of the community in which he lives. Comparatively few medical schools, at the present time, offer courses in experimental pharmacology, and I believe there are no pharmacy schools with the exception of Nebraska. I may be mistaken in this matter and beg to be corrected if I am. My information has been

obtained from the catalogues of the leading American schools and my time has been too limited to write to representative institutions. Experimental pharmacologists are scarcely obtainable at any price because they do not exist. I suppose there are, in the United States, a dozen men who can be called expert pharmacologists, perhaps a few more or less, the number is immaterial. The question is then, how can we install experimental pharmacological teaching in our schools? While experimental pharmacologists are few, physiologists are more plentiful. I believe there are very few State institutions, even in the newer west, that do not have a trained, experimental physiologist. The first prerequisite of a pharmacologist is, of course, that he be a physiologist, and pharmacological work is the legitimate field of the physiologist. No apparatus is needed which is not found in a fairly well-equipped physiological laboratory. I can see no reason why, at least, the fundamentals of experimental pharmacology could not be taught to students of pharmacy. They should, at least, be shown that drugs do induce physiological changes, that these changes are induced by action upon certain part or parts of the organism, and that such action may be used as a means of classification and standardization. If such a movement could be made general, it would give a wonderful impetus to a science which is full of promise for improving both medical and pharmaceutical practice. To me, it is a most significant fact that Ehrlich should, in the prime of his life, turn away from the subject of immunity and serums, to devote practically all of his time to the study of pharmacological problems.

Pharmacy and medicine have a common aim, viz., the conservation of the public health. In recent years we have witnessed a marvelous campaign, waged by the two professions against quackery, graft, disease, and the use of narcotic and habit producing drugs, food preservatives, adulterants, etc. In this work, the leaders of the pharmaceutical profession have taken a place second to medical men. As time goes on, I believe both physician and pharmacist must assume more and more the rôle of the teacher, and co-operate with the teaching profession, and use that profession in disseminating the necessary knowledge to the public. An interesting experiment is being tried in Nebraska, with success. We have a State Teachers' Association of 4000 members. It is composed of twenty-one sections. Two years ago, few philanthropically inclined individuals requested that a section be added to the association,

which should have for its object the discussion of subjects which concern the public health, especially the health of school children. This was done. The section was called the Section on Medical Education. During three days' session of the teachers, many sections must be held at the same time, nevertheless, since its organization 600 teachers have been in attendance at each meeting. The problems are presented to the teachers by the foremost medical and pharmaceutical men of our State, in such a way that the teachers can use the material to advantage in the school-room. I speak of this matter because I believe it is one of the things to which we, as physicians and pharmacists, should give our serious attention. I will admit, however, that I have a certain feeling of pride in the novelty of the scheme.

I would feel justified in giving courses in experimental pharmacology to pharmacy students, if it were for no other reason than that they may see for themselves the harmful effects of the groups of drugs previously mentioned, in order that they may be in a position to authoritatively instruct the citizens of the respective communities in which they dwell.

I am not in sympathy with some recently expressed views that the education of the pharmacist should be broader in order that his field of operation in a professional way be extended, but I do believe in a broader, more thorough, and more scientific training, in order that his efficiency and usefulness may be increased in the field in which he now operates.

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## THE NETHERLANDS PHARMACOPŒIA.\*

BY HENRY KRAEMER.

On recommendation of the Secretary of the Interior, her Majesty, the Queen, decreed, on March 8, 1899, that a commission, consisting of ten members, be appointed to revise the Netherlands Pharmacopœia (*Pharmacopœa Nederlandica*).

The commission as first appointed was constituted as follows: five university professors, two of whom were professors in pharmacy, one a professor in botany, one a professor in chemistry, and one a

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\* Read before the Section on Practical Pharmacy of the American Pharmaceutical Association, May, 1910.



professor in pharmacology; four practical pharmacists, and a chairman, who was the chief of the Board of Health.

The personnel of the original commission was, however, somewhat changed through the death of two members and the resignation of two others, one of whom subsequently died.

Thus, the committee finally responsible for the work of revising the fourth edition of the Netherlands Pharmacopœia consisted of the following members: Dr. H. Wefers Bettink, director of the Pharmaceutical Institute, and professor of pharmacognosy, toxicology, and chemistry, University of Utrecht, chairman; H. P. Wijsman, professor of pharmacy, University of Leiden; J. Gu. Moll, professor of botany, University of Groningen; Gu. Nolen, professor of pharmacology, University of Leiden; Dr. H. Zeehuisen, Army surgeon; P. A. Vos, pharmacist in Rotterdam; C. Guldensteeden Egeling, apothecary in the Province of Zeist; M. J. Schröder, pharmacist of Groningen; L. van Itallie, pharmacist of Rotterdam, now professor in the Veterinary School of Utrecht; Dr. M. Greshoff, director of the Colonial Museum in Harlem.

Before beginning the work of revision proper, the commission asked the national society of medicine and the national society of pharmacy to make such recommendations as they deemed advisable, and they were given until January 15, 1900, in which to consider the matter and formulate their recommendations and suggestions. The commission also took measures to obtain the views of physicians and pharmacists in the Dutch Colonies of the East and West Indies in regard to the manner in which the Pharmacopœia could be improved so as to suit their needs.

After considering the question in all of its bearings they determined to make a pharmacopœia which could be used both in the Netherlands and in the Colonies, giving such alternate formulæ as were necessary to meet the conditions in the Colonies, one of these being the tropical climate. Thus, in the case of ointments requiring 20 to 30 per cent. of adeps or vaseline, provision is made for replacing these bases with *cera flava* or paraffin. In the case of the Indian drugs the local synonyms are appended at the end of the paragraph describing the drug, as, for example, in the case of curcuma, where the synonym, *temoe lawak*, is given.

The commission, after having completed the work of revision, embodied the proposed corrections, additions, and other changes in a supplement, which was published in 1902. Two or three years

were then allowed to elapse in order that the proposed changes might be thought over and their merits and applicability in practice determined. After this preliminary testing of the new Fourth Edition it was published in 1905 and became the official standard on July 1, 1906.

The new work was first printed in Hollandese (Dutch) and then translated into Latin. The Latin edition contains about 550 pages, and is printed in clear type. The book happily combines the results of careful experimental work and improved methods required in the practice of modern pharmacy, and may be said to be the most complete and scientific of any of the national pharmacopœias.

While it is manifestly impossible to consider *in extenso* the various interesting features of the new Netherlands Pharmacopœia in the brief time at my disposal, I shall point out some of the general principles which maintained in the revision of the work, and perhaps call attention to some of the individual drugs and classes of preparations.

One of the notable features of the Netherlands Pharmacopœia, and which makes it a model for an international pharmacopœia, which it is in a certain sense, is that due to the adherence of the commission to the standards adopted by the Brussels Conference for the Unification of the Formulæ for Potent Medicaments. While the agreement for adopting these standards was not signed until November 29, 1906, that is, five months after the Pharmacopœia became official, the standards were practically adopted as proposed by the Brussels Conference in 1902, and the initials "F.I." (Formula Internationalis) are given after the title of each preparation of the potent drugs, as "Tinctura Aconiti, F.I."

The descriptions of the official articles are uniformly complete, rather than what might be termed adequate, as is the case in most of the other pharmacopœias. In practice this is found to be of very great importance, as one is not able to say that a supposedly insignificant character is not of importance at times. If uniform standards mean anything, especially with such potent drugs as aconite and digitalis, for which settled standards have not been provided, it would seem reasonable that the descriptions of the vegetable drugs, as they are the most indefinite substances on the market, should not only be accurate, but fairly complete, so as to preclude the chance for misinterpretation. In the Netherlands Pharmacopœia these

descriptions are frequently as complete as those for the alkaloids and other chemical substances, and in some instances much longer.

The titles for articles and the nomenclature are similar to those in the Third Edition. The main titles of the articles correspond in general to those customarily used in European pharmacopœias, with the exception of the chemical salts, where the acid radical precedes the name of the base, as *iodetum kalicum* for potassium iodide, and *benzoas natricus* for sodium benzoate. While this is contrary to general custom, it may have some advantages, as the physician will find the iodides, benzoates, and so on, grouped together in their respective classes. The titles of vegetable drugs for the most part include a prefix, which indicates the part of the plant used, as *cortex granati*, which title corresponds to the *granatum* of the U. S. Pharmacopœia. Under the principal title a synonym is frequently given, as, for example, *aqua calcis*, the synonym for *solutio hydratis calcici*. Common-name synonyms as we know them in this country are not given, except in the case of the East Indian drugs, already mentioned. This also would seem to have an advantage in that greater uniformity in prescription writing would obtain.

*Vegetable Drugs.*—In the definitions of vegetable drugs it is noticeable that the names of families to which the plants belong are replaced by a citation of the literature giving the original description of the plant, as under *radix ipecacuanhæ*, where we read, "Radices adventiciæ tumefactæ quas præbet *Psychotria Ipecacuanha*, Stokes," Bot. Mat. Med., I, 365 (*Uragoga Ipecacuanha*, Baill. Hist., Pl. VII, 281).

The macroscopic descriptions are complete, and written in such a manner as to indicate that it is expected that dried drugs, such as leaves, will be softened before examination, and frequently the characters described are those requiring the use of a hand lens magnifying five diameters. The histological characters are also carefully described, including descriptions of both longitudinal and transverse sections of a number of drugs.

The powdered drugs are fully described, frequently at considerable length, beginning with the more important and prominent characters and extending to the less characteristic features. The descriptions are based on examinations made with the following reagents: water, chloral hydrate solution, and chloral-iodine solution, and in special cases other reagents may be employed. It is

furthermore directed that if the pharmacist has any question as to the authenticity of the sample examined, he shall compare it with the powder of a drug, the identity of which is known or has been established.

It should be emphasized that this is a very important rule to observe. Considerable stress is laid upon the size of the tissues and cell-contents, and the manner of stating the measurements is quite a novel one.

As every one knows there are certain discrepancies in the literature with regard to the length of fibres, size of starch grains, number of carpels, etc. In order to prepare accurate statements based on statistics which would allow for uncertain variations the latter were arranged in such a manner that the curve of probability would indicate the different possible errors. This is arrived at as follows: The number indicating the minimum size is subtracted from that of the maximum size, and the half of the remainder, known as the quarter (quartilis), is taken to represent the probable mathematical error. The average (or medium) size is obtained either by subtracting the quarter from the maximum or adding it to the minimum. The average size or the average number is indicated by  $M$  and the probable variation above or below this is indicated by  $Q$ , and thus we find under the description of the fibres of powdered cinnamon that  $M$  is equivalent to  $489.5 \mu$  and  $Q$  equals  $55.7 \mu$ , and thus one would expect to find a variation ranging from  $433.8$  to  $545.2 \mu$ .

In those cases where the curve of probability of error would become asymmetric, as in the measurement of potato or maranta starch grains, the size is indicated by an arithmetical ratio represented thus ( $x$ ). Thus under *amylum solani* we find that the error of asymmetry in length of the grain is given as  $23 \mu$ , and is expressed as  $x = 23 \mu$ . This means that after making the measurements of a large number of grains in a certain field, the sum of the sizes of the grains divided by the total number examined gives  $x$ , or the arithmetical ratio.

Again, in the study of starch grains, the position of the point of origin of growth or hilum is indicated by a fraction, the numerator and denominator indicating respectively the distance of the nucleus from the two ends or the two extremes of the longer diameter. Thus,  $\frac{1}{4}$  would indicate that the nucleus is central as in wheat starch;  $\frac{1}{4}$ , as in the case of potato starch grains where the nucleus is  $\frac{1}{4}$  the diameter from the narrow end. In the case of maranta



starch the position of the nucleus is given as  $\frac{1}{1}-\frac{1}{3}$ , meaning that the nucleus is either central or  $\frac{1}{3}$  the distance from the margin to the narrow end in longitudinal section.

In addition to the detailed descriptions of the macroscopic and microscopic characters of the drugs, assay methods are given for many of the potent drugs and statements giving the percentage of ash, amount of extractive, and also other special tests for identity or quality in certain cases.

*Chemical Substances or Medicinal Chemicals.*—In most cases the formula of the chemical is given under the title. A purity rubric is not given, the descriptions and tests being so exact as to establish a high purity of the substance, as is generally the case with foreign pharmacopœias. In the testing of chemicals for impurities, unless a special procedure is given, it is directed that three drops of the reagent shall be added to 5 c.c. of a solution of the chemical. Under *olea pingua* are given a number of general tests for the testing of fixed oils and fats, together with exact methods of procedure in determining the iodine number, saponification figure, and acid equivalent. Under *olea volatilia*, similarly, a general procedure is given for determining the presence of alcohol or fatty oils. In some cases, as under *oleum fœniculi*, the optical rotation is given, and, again, as under *oleum piperita*, a method is given for determining the proximate constituent, menthol. In determining the melting point of fats and fatty substances capillary tubes are used in which the fat is taken up by capillarity after it is melted, and then allowed to stand for twenty-four hours, when the melting point is determined by using a glycerin bath. Specific gravities are determined at a temperature of 15° C. As would be expected  $O = 16$  is taken as the basis for atomic weights, hydrogen being equivalent to 1.008.

*Pharmaceutical.*—The pharmaceutical portion of the book is characterized by the same originality and thoroughness as characterizes the parts already considered. In preparing vegetable drugs for grinding great care is exercised in the drying of the drug, none of the drugs ever being dried above 50° C., and those containing volatile principles not above 40° C., and in some cases over slaked lime. They are then reduced to the fineness required and kept in ground glass-stoppered bottles. Two kinds of sieves are used, one for coarse powders and one for fine powders. In the sieves for coarse powders the meshes are round and are respectively in diameter  $1\frac{1}{2}$ , 3, and 5 mm. These are designated as  $A_{1\frac{1}{2}}$ ,  $A_3$ ,

and  $A_5$ . For fine powders a sieve of silk is used, the meshes being square, there being 10, 20, 30, 40 or 50 meshes in 1 cm. These meshes are indicated as follows:  $B_{10}$ ,  $B_{20}$ ,  $B_{30}$ ,  $B_{40}$ , and  $B_{50}$ . If in connection with an article no fineness is given for the powder, it is intended that the pharmacist shall use a powder of the general degree of fineness designated for certain drugs. Again, there are quite a number of powders which are directed to be kept protected from light and these are indicated by an asterisk (\*). The physical factors which influence the quality or stability of drugs, as light, temperature, moisture, have been given careful consideration. It is directed that all drugs and preparations not in daily use shall be stored in dark rooms and in this connection we note that certain vegetable drugs, as digitalis, are to be kept in tightly closed tin drums in which are placed wide-mouthed bottles containing burnt lime and covered with leather or parchment provided with a suitable number of perforations. It is also directed that hygroscopic chemicals shall be kept in containers with burnt lime. Volatile substances are to be kept in tightly closed glass-stoppered bottles. Chemicals which are affected by the light are required to be kept in black, red, or yellowish-brown bottles. Extracts and ointments are to be kept in jars which do not permit the entrance of light. The commonly used terms relating to temperature in pharmaceutical processes and manipulations all have a definite meaning; thus, when applied to water, *luke-warm* means a temperature of  $20^{\circ}$ – $40^{\circ}$  C.; *warm*, a temperature of  $60^{\circ}$ – $70^{\circ}$  C.; *hot*, a temperature of  $85^{\circ}$ – $95^{\circ}$  C. Again, the temperatures for the processes of maceration, digestion, and infusion are respectively,  $15^{\circ}$ – $25^{\circ}$  C.,  $35^{\circ}$ – $40^{\circ}$  C., and  $90^{\circ}$ – $98^{\circ}$  C.

Standard measures have likewise been adopted. A teaspoonful is defined as equivalent to 3 c.c.; a dessertspoonful as 8 c.c.; and a tablespoonful as 15 c.c., and physicians are requested to adopt the rule of using cubic centimetres when ordering liquid medicines. The standard dropper, approved by the Brussels Conference, has been made official, the dropper having a bore of 3 mm. at the exit end and dropping 20 drops of distilled water at  $15^{\circ}$  C., which should weigh 1 Gm. A table has been included giving the number of drops in a gramme of various liquid preparations and solutions.

In the weighing of drug materials three different grades of scales are directed to be used, which are designated as A, B,  $B_{\infty}$ . Scale A is used in weighing amounts of substances not exceeding

50 Gm., or 10 Gm. with a finer scale. With this scale, which is known as a milligramme scale, the maximum declination or vibration should not be greater than 2 mm. in 1 dm., and not continue longer than one second, when using a weight of 5 mg. Scale B is known as a gramme scale and is used in weighing amounts not greater than 250 Gm., or 100 Gm. with a finer scale. With this scale the sensitiveness should be the same as in Scale A, when using 50 mg. weight. Scale B<sub>2</sub> is used for weighing amounts of substances not exceeding 1 kg., or 250 Gm. with a scale less sensitive than Class B. With this scale the sensitiveness should be the same as in Scale A, when using a 250 mg. weight.

Of the articles official in the Third Edition, 55 were deleted, and 195 new articles were added, making a total number in the Fourth Edition of 652. Of these about 210 are required to be kept in stock at all times by the apothecary. The remaining 442 articles are indicated by a plus (+) sign. In accordance with the Brussels Conference, as already pointed out, the strength of tinctures of potent drugs is 10 per cent.; acidum hydrocyanicum dilutum, 2 per cent.; aqua laurocerasi,  $\frac{1}{10}$  of 1 per cent., or 1 part in 1000, of hydrocyanic acid; the different narcotic extracts and fluidextracts and liquor kalii arsenicosi, 1 per cent.; pulvis ipecacuanhæ opiatu, 10 per cent. of each of the potent drugs; sirupus ferri iodati, 5 per cent.; vinum stibiatum,  $\frac{4}{10}$  of 1 per cent. or 4 per 1000. In order that physicians, as well as apothecaries, shall have in mind the changes in strength of the preparations of potent drugs the abbreviation F.I. (Formula Internationalis) is placed after the title.

In a table (Table A) a list of 42 poisons is given which should be kept in a closet to themselves. In another table a list of poisons is given which may be kept out convenient for use if marked with a label bearing a distinct blue cross. Another table includes medicines which physicians are required to keep on hand. Thus, with the number of drugs and preparations which the pharmacist must always have on hand, and those which physicians are required to keep at hand, the interests of the public are looked after in a manner which seems to be very commendable.

*Doses.*—In order to satisfy the expressed wish of most of the apothecaries of Holland who desired to have a guide that they might follow, the single maximum dose and the maximum dose in twenty-four hours for an adult are given, these being given also in the index, which is, in fact, an alphabetical table giving, in addition, informa-

tion regarding solubility in water and alcohol, and indicating the drugs which are to be kept away from light and those which are to be kept in hermetically sealed containers. If a physician desires to use a larger dose, he is expected to indicate the fact by placing an exclamation point (!) after the name of the medicine specified. These doses hold not only for substances when intended for internal administration but also when administered hypodermically, used in suppositories, or applied to the skin.

*First Help Table.*—In order that the pharmacist may be prepared to act in cases of sudden poisoning there is given in the Appendix an outline of procedure and a list of suitable antidotes which may be easily dispensed by him, he being required to summon a physician as soon as practicable.

The Appendix comprises some eight or nine tables, including (1) general reagents; (2) volumetric solutions; (3) a table of solutions of the alkalies and mineral acids, giving the specific gravity, amount of the chemical in 1000 c.c., and the titration equivalent for each cubic centimetre; (4) a table giving the specific gravity of certain substances at temperatures between 12° and 35° C., as alcohol, ether, chloroform, mineral acids, etc.; (5) a table giving the number of standard drops in a gramme of various potent drugs; (6) an alcohol table; (7) a saturation table; (8) a neutralization table, showing the amount of alkali necessary to neutralize acids or of acids to neutralize alkalies; (9) a table of atomic weights of the common elements.

While it would be desirable for some reasons to compare formula with formula and description with description of the Netherlands and our own Pharmacopœia, this is manifestly impracticable, even with many of the important ones, in a paper of this kind. I will, however, consider a few of the minor or detailed features.

Not only has the Netherlands Pharmacopœia adopted the standards of the Brussels Conference for tinctures of potent drugs but also for certain alkaloids, as the hydrochlorate of cocaine, the title of which is hydrochloras cocaini, F.I., which means that it shall answer the original MacLagan's test for other coca alkaloids, and in addition to other tests there is a method given for the detection of cinnamyl ecgonine.

Under the various galenicals, as tinctures, various data are given for their identification and test of purity, as color, specific gravity, amount of extract, and certain specific tests. In the preparation of tinctures, unless a special method is given, either percolation or



maceration may be used. When maceration is followed, the comminuted drug is mixed with the proper quantity of the menstruum, allowed to macerate five days with occasional agitation, and protected from light. The marc is pressed out and the liquid portion allowed to stand in a cool place for two days, when it is filtered, care being taken to prevent evaporation. In following out the percolation method the menstruum is divided into three parts, two of which are intimately mixed with the drug, allowed to macerate for twelve hours. This macerated mixture is then added to a percolator and slightly compressed. Sufficient menstruum is added until the percolate begins to flow from the orifice of the percolator, the latter is then closed and the drug allowed to macerate for 24 hours. The stopper is removed and percolation allowed to proceed, and as much menstruum added as is necessary to make the required amount after expression of the marc. The tincture is allowed to stand for two days in a cool place, when it is filtered, taking care to avoid loss by evaporation.

All of the tinctures of potent drugs are made by percolation, while all of the remaining tinctures are made by maceration. In the case of *tinctura secalis cornuti* and *tinctura strychni*, the fixed oil is first removed from the drugs by means of petroleum ether. There is also a general test given for the detection of wood alcohol and acetone in tinctures.

Three classes of extracts of vegetable drugs are recognized: dry extracts or *siccum* (*extracta sicca*), which contain not more than 6 per cent. of moisture; solid extracts, or *extracta spissa*, which contain not more than 20 per cent. of water, and liquid extracts. The extracts of potent drugs are made by percolation in much the same manner as given for tinctures, the alcohol being removed either by distillation at a temperature not higher than 90° C., or it may be allowed to evaporate spontaneously until the extract has the desired consistency. Most of the extracts of the other drugs are made by maceration or infusion, it being understood that the processes are carried out at definite temperatures, considerable care being directed in the evaporation of the extracts. In *extractum secale cornuti*, chloroform is used as a menstruum; in a number of extracts a certain amount of glycerin is directed, as with *cinchona*. With the latter drug dilute hydrochloric acid forms a part of the menstruum. In preparation of the liquid extract of *hydrastis* tartaric acid is added to the menstruum. Methods are given for the determination of moisture, the examination of the ash for metallic

substances, and they are required to be protected from light, and in view of their containing soluble constituents, to be kept in glass-stoppered bottles.

It is rather surprising that in view of the increasing use of so-called animal drugs in this country, as antitoxins, etc., none of these articles are official in the Netherlands Pharmacopœia. This is probably accounted for by the fact that one of the principles of revision is not to include any substance, no matter how widely used it may be, which the pharmacist does not prepare or has no adequate means of testing. Neither are patented or trade-marked preparations official, the entire responsibility for their quality resting with the manufacturer. On the other hand, formulæ are given for the preparation of teas (species); artificial aperient salts, as Carlsbad salts; medicated cottons and gauzes; granules, and so on. Indeed there are methods for every class of pharmaceutical preparations from aquæ to vinæ, and with standards or tests for every substance and preparation used.

Everything that science or experience can offer is at the disposal of the physician, and the pharmacist cannot misunderstand the specifications of the physician or fail to supply uniform and efficient preparations.

I may in conclusion say that the Netherlands Pharmacopœia is not only a very valuable practical guide for the retail pharmacist, but that it furnishes high standards for the official drugs, the revisers having availed themselves of the scientific progress touching their work and having also manifested a broadly democratic spirit. We have also in the Netherlands Pharmacopœia a standard, which while revised by authority of the Government, yet strictly speaking none of the members of the commission are Government officials. The commission is a small one, and the members are directly responsible for the work.

The Japanese have used it as a model since 1880, and it would be well if an English translation were available for consultation and study in this country.

Finally, I acknowledge my indebtedness to Mr. Peter Amsterdam for assistance in translating and critically examining certain portions of the Latin edition. I have also had access to two excellent reviews of this work, one by Schoepp in the *Apotheker Zeitung* for 1906 and 1907, and another by Weigel in the *Pharmaceutische Zentralhalle* for 1906.

## SHALL WE HAVE A PROFESSION OF PHARMACY?

BY F. E. STEWART, PH.G., M.D.

The following is abstracted from my lecture on the above subject delivered recently before the Philadelphia College of Pharmacy and the Medico-Chirurgical College of Philadelphia. This abstract represents the lecture very incompletely; and, as the subject is fundamental and vital to the existence of pharmacy as a profession, the entire lecture, which will be published later,<sup>1</sup> should be read.

Pharmacy, or the art of preparing medicine, is historically and in fact a branch of medical science and practice. Like theology, law, and medicine, pharmacy was originally practised by the priests. Advance in civilization finally segregated the vocation of the priest; and theology, law, and medicine became separate professions. The segregation was accomplished gradually. The priests practised medicine, surgery, and pharmacy. In England this was the case.

In 1215, the priests in England were forbidden to practise any surgery which involved the shedding of blood. About a century later all forms of surgery were forbidden them, and thus began the division between medicine and surgery which still continues.

The physician was still the pharmacist, until chemistry was born of alchemy, and its application to the study of *materia medica* rendering pharmacy more complex, it was finally relegated to the apothecaries, who in those days were members of the Guild of Grocers, the vocation not being of a professional character. In 1607, under the title of the "Apothecaries of the City of London," the apothecaries separated from the grocers, and appear to have prescribed medicines in addition to dispensing them, claiming an ancient right of acting in this double capacity, although theoretically the apothecary was the humble servant of the physician, merely preparing the medicines ordered by the latter.

When the priests or monks ceased to practise surgery, the barbers, who had acted as their assistants, usually ignorant and venal in the extreme, practised alongside of the surgeons proper. In the sixteenth century, medicine being still largely a priestly vocation, Linacre, a celebrated divine, physician to Henry the Eighth, founded,

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<sup>1</sup> Published in *Pharmaceutical Era*, May, 1910.

in England, the present College of Physicians, which, together with the Universities of Oxford and Cambridge, where medical schools had been established, received authority over all three branches of medicine.

It is worthy of note that whereas physicians qualified for their degrees by study at the universities, surgeons and apothecaries obtained their qualifications by apprenticeship (seven years apprenticeship being required for membership in the Apothecaries' Society), and apothecaries and surgeons were, therefore, ranked socially with tradesmen or members of other crafts, while physicians held the higher rank of membership in the learned professions.

In 1666, the Great Plague broke out in England, and although many physicians stood nobly at their posts, many more fled in terror. The sick, therefore, fell back upon the apothecaries, who distinguished themselves by their courage and humanity, and from this time on there seems to have been an increased tendency upon the part of the apothecary to assume the prerogatives of the physician.

A warm contest arose between physicians and apothecaries, the former accusing the latter of usurping their province, and the latter continuing and justifying the usurpation, until the dispute was finally set at rest, in 1703, by a judgment of the House of Lords. It was decided that the duty of the apothecary was not only to compound and dispense but also to direct and order the remedies used in the treatment of disease. He was allowed no right to charge for his services, but was to rely entirely on his medicines for his profits. In 1815 was passed an Act clearly contemplating "the creation of a class of practitioners who, while having the right to practise medicine, should assist and co-operate with the physicians and surgeons." The Act of 1874 "gave power to the Apothecaries' Society to unite or co-operate with the medical examining boards in granting licenses to practise." According to the *Encyclopædia Britannica*, from which I drew some of my information regarding the status of pharmacy in England, the term "apothecary" indicates a general practitioner who supplies drugs to his patients.

The "status of the apothecary in America" is still in the formative state, the process of formation being in rapid evolution. To understand the significance of the epoch-making events which have transpired in this country during the past decade, together with their probable effect upon the pharmacy of the future, it is necessary to consider more in detail the:



TRUE IDEAL OF PROFESSIONAL PHARMACY.

The term "profession of pharmacy" implies a fraternity of pharmacists holding as common property the results of the experience of the profession. According to the professional ideal, each pharmacist should manufacture and deal in the same pharmaceutical preparations, under the same names, made according to common standards and by the same methods; and each member of the profession is supposed to devote a portion of his time to original research and to publish the results of his observations for the benefit of science, that the fraternity may have free use of the same.

I called attention to the fact that the results of such researches, when reduced to law and embodied in system, constitute the "science of pharmacy," or, more properly, the "science of pharmacology." Pharmacology is defined by the National Syllabus Committee to be "The sum of scientific knowledge concerning drugs and medicines; their nature, preparation, administration, and effect; including pharmacognosy, pharmacy, pharmacodynamics, and therapydynamics." According to this same authority, "Pharmacy is a branch of pharmacology, including the science and art of preparing and dispensing medicine." These definitions are not new ones, being supported by H. C. Wood, in his text-book on *Materia Medica*, also by Hermann, in his "Experimental Pharmacology," and by the various dictionaries, but I will not take space here to give the full quotations I gave in my lectures.

According to the National Syllabus Committee's definitions, pharmacology embraces a knowledge of the following subjects: Drugs, medicines, *materia medica*, chemistry, pharmacy, physiology, botany, microscopy, pharmacognosy, toxicology, posology, elementary physics, manufacturing chemistry, pharmaceutical arithmetic, pharmaceutical latin, theory of pharmacy, practice of pharmacy, commercial pharmacy, manufacturing pharmacy, histological pharmacognosy, pharmacodynamics, therapydynamics, assaying, dispensing pharmacy, and pharmaceutical jurisprudence.

According to the Standard Dictionary, "Science is knowledge reduced to law and embodied in system." Therefore, the knowledge of the above-mentioned subjects, when systematically arranged, constitutes the "science of pharmacology." The same authority states "Knowledge of a single fact, not known or related to any other, or of many facts not known as having any mutual relations or com-

prehended under any general law, does not reach the meaning of science." Pharmacy, as previously defined, is, therefore, not sufficiently comprehensive to justify dignifying it as a science.

The logical conclusion is that the terms "Profession of Pharmacology" and "College of Pharmacology" are to be preferred to the less comprehensive terms now used.

#### HOW THE PROFESSIONAL IDEAL IS TO BE REALIZED.

Progress in pharmacologic science and practice is dependent upon four essential features; namely, organization, co-operation, standardization, and legislation.

*Organization.*—It is evident that the true professional ideal includes the organization into one association or fraternity of all persons devoted to the science of pharmacology or engaged in the practice of the pharmacologic arts. Such an association would include pharmacists engaged in retail, wholesale, and manufacturing drug business, the pharmaceutical chemists connected with the laboratories of manufacturing houses, and the teachers in medical and pharmaceutical schools working in the field of pharmacology. And, as pharmacotherapy is dependent upon pharmacology, physicians interested in that branch should also be included.

The American Pharmaceutical Association approaches more nearly to being such an organization than any other now existing, and could be made to cover the field by broadening its work to include pharmacodynamics and therapydynamics, and later to include pharmacotherapy also. The work of the National Syllabus Committee has become part of the work of the Section on Education and Legislation of the American Pharmaceutical Association, and I would suggest that the report of the committee (pages 750-58 of the Proceedings of the A. Ph. A. for 1908) is worth most serious consideration by all teachers and students of pharmacy.

*Co-operation.*—Progress in pharmacologic science and practice requires co-operation between practitioners of the pharmacologic arts and the medical profession. Unless the medical profession employs, in treating the sick, the medicines properly prepared by professional pharmacologists, of what use is a profession of pharmacology? The pharmacologist is not educated to diagnose and treat disease, and when he ignorantly prescribes medicines for self-medication he is a menace to public health and should be suppressed. Either the pharmacologist to be evolved by the operation of the

educational system proposed by the National Syllabus Committee will have to know enough of medicine to warrant his intelligently prescribing and recommending medicines, or the medical profession will have to be educated to appreciate a true profession of pharmacology. Both suggestions appeal to me as worthy of consideration.

*Standardization.*—The professional ideal includes a pharmacopœia, dispensaries, text-books, and colleges of pharmacy or pharmacology. Until the Pure Food and Drugs Act of June 30, 1906, went into effect, conformity with the standards of the U. S. Pharmacopœia was purely voluntary. This was an excuse for each manufacturer, little or big, to set up a standard of his own, and the ill effects resulting therefrom have given rise to the condition of mind on the part of physicians known as therapeutic nihilism. The enforcement of the federal Act mentioned, aided by State legislation of the same sort, will do much toward overcoming the ill effects of lack of standardization. The final end of any product worthy of consideration as a therapeutic agent should be its incorporation into the U.S.P. or N.F.

*Legislation.*—One of the most important suggestions regarding pharmacal and medical legislation ever made in this country is to be found in the decision of the Supreme Court of the United States, in the case of Worden vs. the California Fig Syrup Co., No. 35, October Term, 1902, as follows:

“Many, if not all, of the States of this Union have enactments forbidding and making penal the practice of medicine by persons who have not gone through a course of appropriate study and obtained a license from a board of examiners; and there is similar legislation in respect to pharmacists, and it would seem to be inconsistent and to defeat such salutary laws, if medical preparations, often and usually containing powerful and poisonous drugs, are permitted to be widely advertised and sold to all who are willing to purchase. Laws might properly be passed limiting and controlling such traffic by restraining retail dealers from selling such medicinal preparations, except when prescribed by regular medical practitioners.”

The foregoing decision would force retail druggists to practise therapeutics or entirely discontinue the recommending of medicines, and as it would be practically impossible to carry on the retail drug business without the privilege of recommending medicines to persons coming to the drug store for the treatment of minor complaints,

it would, therefore, be the part of wisdom to arrange that such treatment should be given intelligently and in accordance with proper legal restrictions, not as a commercial business, but as a branch of medical practice under control of medical laws.

#### FUNCTION OF THE PHARMACOLOGIC PROFESSION.

The function of the pharmacologic profession shall be:

- I. To promote progress in the science of pharmacology and the practice of the useful arts of pharmacognosy, pharmacy, pharmacodynamics, and therapydynamics.
  - a. By investigating the substances from all parts of the world, which are, or may be, used as medicines, and introducing them to science and commerce.
  - b. By devising methods for their identification, selection, preparation, preservation, compounding, and dispensing.
  - c. By adopting and maintaining standards for their protection against adulteration, sophistication, and fraudulent substitution.
  - d. By legislation for the protection of standards (pure food and drug laws); for the protection of the profession from encroachments from without upon its field (pharmacy laws); for the protection of the profession from malpractice on the part of its members (code of ethics); to protect materia medica science and commerce (copyright, patent, and trade-mark laws).
2. To co-operate with the medical profession in the prevention of disease and the treatment of the sick.
  - a. By refraining from encroachment upon the field of medical practice.
  - b. By refraining from advertising medicines for self-medication.
  - c. By taking an active part in educating the public against the abuse of drugs.
  - d. By acting as a medium for the dissemination of information in relation to the prevention of communicable disease, such as tuberculosis, smallpox, etc.
3. To practise the pharmacologic arts by selecting, preparing, preserving, compounding, and dispensing medicines, in accordance with professional and scientific requirements.



PERSONNEL OF THE PHARMACOLOGIC PROFESSION.

The pharmacologic profession shall consist of licensed physicians especially interested in materia medica, either as practitioners, teachers, or laboratory workers; graduates of pharmacy engaged in the retail or wholesale drug business or in the manufacturing chemical or pharmaceutical industries; pharmaceutical chemists with degrees from reputable schools or universities; botanists specially interested in pharmacognosy, and members of botanical societies in good standing; physiologists engaged in pharmacodynamic investigation and materia medica standardization; bacteriologists connected with laboratories for the production of biological materia medica products, or their investigation and standardization; and government experts in any way associated with departments engaged in the identification, or standardization, of drugs, or the study of medicinal plants and their agriculture.

CO-OPERATE INVESTIGATION OF THE MATERIA MEDICA AND  
INTRODUCTION OF NEW PRODUCTS.

Progress in pharmacologic science can be attained only through co-operative materia medica investigation, the results of which, according to professional ideals, belong not to the individual investigators but to the profession. Members of the pharmacologic profession, with the exception of teachers and government experts, should be supported by materia medica commerce, hence it is essential that such commerce shall be a professional vocation, that pharmacologists supported by commerce shall be considered scientists and entitled to rank with the members of the medical profession.

PURE FOOD AND DRUG LAWS.

The Pure Food and Drugs Act protects materia medica standards not only directly, but indirectly, by forcing manufacturers to label their products truthfully. Although, with few exceptions, drugs are not specifics, both retail and wholesale manufacturers of medicines have long advertised their products as "cures," and it is by means of these false claims that the so-called proprietary medicine business has reaped such a rich harvest. By ruling against the use of the word "cure" on labels the Government has dealt a solar plexus blow to such fraudulent exploitation of the public. Moreover, the

public is growing wiser, and no longer believes the advertisements of the nostrum manufacturers.

Recognizing the limitations of drugs as therapeutic agents, many persons are seeking in Christian Science, Osteopathy, the Emanuel Movement, Psychotherapy, etc., the relief not afforded by doctors and druggists, with results disastrous to the drug business and the medical profession. For this condition two remedies are suggested, one being that druggists should have the same faith in their drugs that Christian Scientists have in the doctrines of Mrs. Eddy and should inspire the public with such faith, giving their patrons the benefit of suggestive therapeutics; in other words, druggists are to become quack doctors and resort to pretense as a therapeutic agent.

The other remedy is the plan I have been advocating; namely, that pharmacists study medicine and obtain a license to practise therapeutics, taking advantage of their close contact with the people to educate them on the subject of medicine, that they may learn to avoid the numerous pitfalls for the unwary set by quacks and pretenders of all kinds. Aided by the enforcement of pure food and drug laws, this plan would doubtless prove of the greatest value to mankind and do more than anything else yet suggested to raise pharmacologic practice to its proper position as a learned and beneficent profession. What we need, and what the public is going to have sooner or later, is an honest pharmacologic service, and if physicians and pharmacists will co-operate in this endeavor the confidence of the public in medicine and pharmacy will be restored.

#### ENCROACHMENT OF THE MANUFACTURING HOUSE.

Many retail druggists object to the pure food and drug laws. They claim that the manufacture of medicine is the exclusive right of the retail druggists, and that the enforcement by the courts of standards for materia medica products is taking from the retailers their business as manufacturers and placing it in the hands of the great commercial houses, which are conducted by a non-professional body of men who do not hesitate to sacrifice the public for gain.

*(To be continued.)*

## HYGIENIC LABORATORY BULLETINS.

In addition to Hygienic-Laboratory Bulletin No. 63, commented on in this JOURNAL for October, 1910 (p. 495), at least four of the recently issued bulletins contain information that will be of interest and value to pharmacists.

It should be remembered that all applications for these publications should be addressed to the " Surgeon-General, U. S. Public Health and Marine-Hospital Service, Washington, D. C."

HYGIENIC LABORATORY BULLETIN No. 69. The effects of a Restricted Diet and of Various Diets upon the Resistance of Animals to Certain Poisons. By Reid Hunt. Washington, Government Printing Office, 1910, p. 89.

This bulletin contains reports of experiments and observations on a subject that promises to be of very great importance in the study of the action of medicines. In the course of his experimenting Hunt has observed some very striking alterations in the resistance of animals to certain poisons produced entirely by changes in diet. Thus of animals kept upon diets such as are in daily use by man some were able to resist many (up to 40) times the amount of certain poisons fatal to animals kept upon other diets. He points out that although the results with certain of these poisons probably have no relation to man, yet they show that man is doubtless daily producing profound effects upon his resisting power to poisons and diseases, a knowledge of some of which may be of much practical importance. It seems certain that by the use of some of these reactions changes in metabolism, which are not recognized by the methods ordinarily employed, may be detected.

As noted above, the experimental data recorded in this bulletin will no doubt be of value in stimulating investigation on the relation of diet to the physiologic and therapeutic action of remedial substances as well as the more direct toxic action of potent medicaments.

HYGIENIC LABORATORY BULLETIN No. 67. The Solubilities of the Pharmacopoeial Organic Acids and Their Salts. By Atherton Seidell. Washington, Government Printing Office, 1910, p. 93.

This bulletin contains records of experimental work done to determine the solubility in water and aqueous alcohol solutions of some 40 or more official substances.

The experimental methods employed are described in detail and the results are given in the tables in all cases in the terms in which solubility data are usually expressed in the chemical literature, and in addition the equivalent values are expressed as customarily found in the pharmaceutical literature, *viz.*, the amount of solvent required to dissolve a unit amount of the dissolved substance. Seidell points out that although this latter mode of expressing solubility results has been used for many years by pharmacists, it is unscientific and not even as useful for practical purposes as the percentage basis adopted by chemists. As an illustration, pharmacists are usually called upon to compound their mixtures in certain definite amounts, and, therefore, the quantity of the dissolved substance which will be contained by the given volume of the solution is certainly of more practical interest to them than the knowledge of the amount of the solvent required for one part of the given substance. It would therefore appear of considerable advantage to pharmacists to abandon their antiquated mode of expressing solubility results and adopt the more rational percentage or unit of solvent basis in their pharmacopœias and pharmaceutical reference books.

HYGIENIC LABORATORY BULLETIN No. 66. I. The Influence of Age and Temperature on the Potency of Diphtheria Antitoxin. By John F. Anderson. II. An Organism (*Pseudomonas protea*) Isolated from Water, Agglutinated by the Serum of Typhoid Fever Patients. By W. H. Frost. III. Some Considerations on Colorimetry, and a New Colorimeter. By Norman Roberts. IV. A Gas Generator, in Four Forms, for Laboratory and Technical Use. By Norman Roberts. p. 104.

The contents of this bulletin are fully indicated by the titles of the several contributions enumerated above.

The paper by John F. Anderson is a comprehensive and timely review of work done on the keeping qualities of diphtheria antitoxin and a report of experiments made in the Hygienic Laboratory with 18 different lots of serum furnished by 14 different manufacturers. Anderson concludes that: "The average yearly loss in potency of diphtheria antitoxin at room temperature is about 20 per cent.; at 15° C., about 10 per cent.; at 5° C., about 6 per cent., although in some instances these percentages may be much increased.

"From this work, there appears to be but little difference in the



keeping qualities of untreated sera and sera concentrated by the Gibson process.

"Diphtheria antitoxin to be placed upon the market and there kept under unknown conditions as regards temperature should not be labeled with a return date longer than two years and should contain an excess of at least 33 per cent. to allow for decrease in potency; in addition, when the serum is sold in syringes with an absorbable piston, an excess should be added for this loss.

"Dried diphtheria antitoxin, kept in the dark, at 5° C., retains its potency practically unimpaired for at least five and one-half years.

"The lack of confidence in the therapeutic properties of old sera is without basis, as such sera, unit for unit, are as potent as new sera.

"The protective value of diphtheria antitoxin is in exact accord with its unit value and is independent of the volume of the serum or other properties in the serum."

The two contributions by Norman Roberts are also of interest to pharmacists engaged in laboratory work. The colorimeter described should prove to be useful and more economical in construction than any of the instruments of this kind now available.

The gas generator in the several forms described would appear to meet the requirements for which they were designed and are suggestive of simple modifications that could be adapted to the everyday needs of any laboratory.

HYGIENIC LABORATORY BULLETIN No. 65. Facts and Problems of Rabies. By A. M. Stimson. Washington, Government Printing Office, 1910, p. 85, pl. V.

This bulletin, while by no means pharmaceutical in nature, is, nevertheless, of interest to pharmacists because of the complete way in which a much dreaded disease is described and methods for its prevention or complete eradication outlined.

After comprehensively reviewing the history, prevalence, pathology, and etiology of rabies, Stimson discusses its prevention and treatment and concludes, in part, that: "It is apparent that the disease is quite prevalent in the lower animals and not as rare in man as has been supposed. Exact information as to its prevalence in the United States is not available and its acquisition is necessary.

We have a good deal of data on the pathological findings of the disease, but there are many points concerning its essential pathology that require elucidation. We know that rabies is caused by a living micro-organism which invades the nervous system and can be thrown off in the saliva. The exact nature of this organism is still unknown.

"The treatment of developed rabies by means of drugs, while it has received considerable attention in the past, perhaps because of the discouraging outcome of the earlier attempts at treatment, has received but little attention in recent years. In view of the facts that the balance of evidence leans toward the protozoan nature of rabies, and that certain protozoan infections are amenable to cure by specific drugs, it is our opinion that research in this direction should not be abandoned. The most promising line of investigation in this connection would appear to be based not upon the physiological action of the drug, but upon its action upon the parasite. Here we are limited at once by our lack of knowledge.

"Attempts to improve upon the methods of immunization of exposed persons are desirable, in order to eliminate the small percentage of failures and the very much smaller proportion of injurious results. In making such attempts, however, we must not jeopardize human life by the use of methods which are without experimental basis.

"Finally, as regards the eradication of rabies, we have now and have had for a long time all the knowledge of rabies necessary to effect its entire suppression. This knowledge can be summed up in a single sentence, to wit: Rabies is perpetuated in the dog through the infliction of bites by a rabid dog and does not arise spontaneously. If all rabid dogs could be prevented from biting other animals, rabies would in the course of a year be a mere historical curiosity of medicine, an illegitimate field of research for the investigator in pure pathology, a plaything for the controversialist."

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## BOOK REVIEWS.

ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITÄT BERLIN. Herausgegeben von Dr. H. Thoms, Professor und Direktor des Pharmazeutischen Institutes der Universität Berlin. Siebenter Band. Umfassend die Arbeiten des Jahres, 1909. Mit 6 Textabbildungen und 7 Tafeln. Berlin, Urban & Schwarzenberg. 1910. Paper 7 Marks. Cloth 8.50 Marks.

This volume of 312 + VIII octavo pages represents a compilation of the work done in the pharmaceutical institute of the University of Berlin during the year 1909, and, with the six preceding volumes, constitutes a record of accomplishment of which any institution might well be proud.

As has been pointed out before the work done in connection with the pharmaceutical institute of the University of Berlin is unique and the institution is not alone a pharmaceutical school and a laboratory for original research, but, to a lesser extent perhaps, also a central station for the control of new remedies and proprietary medicines.

From a practical point of view this activity is by no means the least important of the several activities of the institute and, in the recently published report, readily surpasses all of the other departments in number of communications.

It may be well to add that this particular branch of the activities of the institute is being conducted at the expense of the German Society of Apothecaries and that the work itself has much in common with the work done by the Council on Pharmacy and Chemistry of the American Medical Association. Indeed, the director of the Institute, Prof. H. Thoms, has for some years been affiliated with the Council as a corresponding member and the work of the Berlin Institute is frequently quoted in the pages of the *Journal of the American Medical Association* and has been of practical assistance in the detection of irregularities in connection with European specialties.

While the reports of work done in the institute at Berlin are frequently mentioned or abstracted in this JOURNAL as well as in the *Journal of the American Medical Association* it is perhaps unfortunate that the contributions, as they are gathered together in the volume under discussion, are not more readily available to the average pharmacist in this country.

As an illustration of the varied character of the information that is supplied, and as an indication of the nature of the work that is being done by the men who are officially connected with the pharmaceutical institute of the University of Berlin, it may suffice to enumerate the contents of the volume before us.

In addition to a general review of the new remedies and proprietary specialties introduced in 1909, the book records the examination of 30 new remedies and proprietary specialties and contains in

addition 1 article on the testing of quinine pills, 5 articles bearing on phytochemical subjects, 12 articles of a general chemical character, 12 articles on technical and food products from the colonies, 1 article describing an extraction apparatus for a variety of purposes, and a reprint of a lecture by the director on sources of energy for chemical processes.

In Europe the work done in connection with the pharmaceutical institute of the University of Berlin has served as an incentive for other institutions to follow in the same lines and work of a similar nature is now being done in connection with the pharmaceutical institutes of other German Universities, and also, to a lesser extent perhaps, at similar institutions in Austria, Switzerland, France, and Holland.

With the interest that is being evidenced in the work of the Council on Pharmacy and Chemistry of the American Medical Association, and the evident reawakening on the part of pharmacists to an appreciation of the uses and limitations of official drugs and open formula preparations, we will, in the very near future, no doubt, witness the development of similar work on the part of schools and colleges of pharmacy in the United States. M. I. W.

HANDBUCH DER PHARMAKOLOGIE. Von A. Tschirch. Mit zahlreichen Abbildungen im Text und auf Tafeln sowie mehreren Karten. Lieferung 19-21. Leipzig: Chr. Herm. Tauchnitz.

Beginning with Part 19, we have the second part of Tschirch's Hand-book, dealing with Special Pharmacognosy. As the pharmacologist desires to know the nature of the active principles of drugs, Tschirch classifies them according to their chemical constituents. The first group considered are the carbohydrates, among which we find Mel, Flos Verbasci, Caricæ, Dactyli, Passulæ, Fructus Juniperi, Fructus Sambuci, Fructus Pruni, Fructus Jujubæ, Fructus Myrtilli, Fructus Rubi Idæi, Radix Liquiritæ, Manna, Saccharum, Amylum, etc., etc.

Each product or drug is considered in detail as follows: Synonyms, etymology, botanical origin, description of the plant yielding the drug, and the diseases which may affect it, cultivation, source, commercial varieties, macroscopic and microscopic description of the drug, chemical constituents, adulterations, historical notes concerning the drug, and a nearly complete citation of the important literature.



The monographs of the different drugs are very complete and while one does find a number of omissions, as for instance under *Glycyrrhiza*, in the enumeration of other plants containing glycyrrhizin, this is rather to be expected, as the task undertaken by Tschirch is almost superhuman.

The amount of information collated of each drug, the nearly complete citation of the literature, and the numerous excellent illustrations make this work indispensable to both the pharmacist and pharmacologist.

H. K.

PHARMAKOLOGISTISCHER ATLAS. Zweiter Teil der mikroskopischen Analyse der Drogenpulver. Erster Band. 1. Lieferung. Von Dr. Ludwig Koch, Universität Heidelberg. Leipzig: Verlag von gebrüder Borntraeger, 1909.

In this part of Koch's excellent Atlas we find microscopic descriptions of the following barks: *Cascarilla*, red cinchona, and cinnamon. The illustrations are well drawn and quite accurate. Pharmacists, and particularly pharmacognosists, are indebted to Dr. Koch for giving us such a painstaking and valuable work.

H. K.

THE ECLECTIC ALKALOIDS, RESINS, RESINOIDS, OLEORESINS, AND CONCENTRATED PRINCIPLES. By John Uri Lloyd. Bulletin of the Lloyd Library, No. 12. Pharmacy Series, No. 2, 1910. Cincinnati: J. U. and C. G. Lloyd.

This is a very valuable publication, and there is probably no one living who could present in such a concise and illuminating manner the history of the "Concentration feature of the American *Materia Medica*" as the author. He says: "It will be perceived that the so-called eclectic resinoids, alkaloids, and resins were introduced into the passing along of the science of pharmacy, *materia medica*, and medicine of the nineteenth century, much as a foreign body, for a temporary purpose, becomes a part of a structure from which it is afterwards excised, leaving in the end a few remnants only to tell the story of its former usefulness. It is as the superstructure to a bridge that, supporting the incomplete edifice, is vital to its very construction, but yet is finally torn away by its own builders."

In the present volume are excellent portraits and brief biographies of John King, William Stanley Merrell, Alexander Wilder,

William Tully, Grover Coe, Robert Stafford Newton, Edward S. Wayne, Calvin Newton, and John Coakley Lettsom.

This Bulletin of the Lloyd Library will always be consulted by the historical students in pharmacy and medicine with great interest and profit, although the author considers it "as merely an introductory chapter" regarding the record of American *materia medica* and pharmacy.

H. K.

SERUM DIAGNOSIS OF SYPHILIS and the Butyric Acid Test for Syphilis. By Hideyo Noguchi, Associate Member of the Rockefeller Institute for Medical Research, New York. 14 Illustrations. Philadelphia and London: J. B. Lippincott Company.

"The object of this book," as stated by the author, "is, first, to give a brief yet adequate account of the principles of serum hæmolysis and of the behaviors of the combinations of antigens and antibodies towards hæmolysis, so essential for a proper understanding of the subject, discussing at some length the quantitative relationship of the factors playing a part in these phenomena, an aspect of the subject that has perhaps not received the consideration that it deserves; and, secondly, to give in detail the technic of Wassermann's method and of the method recommended by the author."

The presentation of the subject by the author is logical and unusually clear, so that this work can be used as a laboratory guide by the student and medical practitioner. From the numerous confirmatory results obtained by Dr. Noguchi it would appear that the butyric acid test is a useful addition to the diagnostic methods in the detection of parasyphilitic diseases of the central nervous system and of cerebrospinal syphilis.

H. K.

FUNGUS DISEASES OF PLANTS. With chapters on Physiology, Culture Methods, and Technique. By Prof. Benjamin M. Duggar, New York State College of Agriculture, Cornell University. Boston: Ginn and Company.

While there are several good foreign books dealing with plant diseases, there has not been available a work which deals with American conditions and takes cognizance of the large number of investigations on plant pathology which have been carried on in this country.

The present book is intended as a general text and reference book for the student and plant producer. In the discussion of each plant disease the following considerations have been kept in view: (1) to describe the pathological effects and other relations of host and parasite; (2) to make clear the life history of the casual fungus; and (3) to indicate the approved or suggested methods of prevention or control.

The illustrations are numerous and excellent. There is also a valuable extensive host index in which is presented in a succinct form all the diseases discussed to which the host plants are subject.  
H. K.

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## PHILADELPHIA COLLEGE OF PHARMACY.

### MINUTES OF THE SEMI-ANNUAL MEETING.

The semi-annual meeting of the College was held September 26, at 4 P.M., in the Library. Eighteen members were present. In the absence of the President, Howard B. French, who was in the far West, the Second Vice-President, Joseph L. Lemberger, presided. The minutes of the quarterly meeting held June 28 were read and approved. The minutes of the Board of Trustees for June were read by the Registrar, J. S. Beetem, and approved.

The report of the Committee on Nominations was read and ordered filed. A letter was read from Mr. Samuel C. Henry, who had been nominated to the Board of Trustees, thanking the Committee for the nomination and expressing his appreciation of their action, yet requesting the members present to vote for the other nominees who had previously served as Trustees, as they had served the College faithfully and well.

The names proposed for Honorary Members at the meeting in June and laid over till this meeting were then elected as Honorary Members, as follows: Wilhelm Ostwald, formerly Professor of Chemistry at the University of Leipzig, Germany; Josef Moeller, Professor of Pharmacology and Pharmacognosy at the University of Graz, Germany; H. Wefers Bettink, Director of the Pharmaceutical Institute of the University of Utrecht, Utrecht, Holland; C. E. Bessey, Professor of Botany, University of Nebraska, Lincoln, Nebraska.

ELECTION FOR TRUSTEES.—William McIntyre and William E.

Lee were appointed tellers, who after a ballot was taken, reported the election of E. M. Boring, Theodore Campbell, and Charles Leedom to membership in the Board of Trustees for the ensuing three years.

While the tellers were counting the ballots, Mr. William L. Cliffe informed the members as to the progress being made in preparing for the new course in physical training. The upper floor was almost ready, and when completed would compare favorably with other institutions that had devoted much time to athletics. The Medical Examiner and the Instructor in Physical Training were anxious to do their part of the work for the work's sake and because of their belief in the great value of athletics in educational institutions. The eyes of the students will be especially examined by an expert, without additional cost to the College, and it is expected that this examination of the eyes will prevent much future trouble by an early recognition of eye defects.

Messrs. Lemberger, Kraemer, Remington, and Boring expressed their pleasure at the information given by Mr. Cliffe.

The Chairman reappointed the Committee on Membership, as follows: C. B. Lowe, Chairman, Martin I. Wilbert, Edwin M. Boring, Richard M. Shoemaker, C. A. Weidemann.

Professor Henry Kraemer stated that the report of the delegates to the Pennsylvania Pharmaceutical Association meeting held at Buena Vista Springs, June 28-30, had been overlooked, and in the absence of the Chairman, Dr. C. B. Lowe, he asked to furnish a report for record and that it be recorded as of the minutes of the meeting. Dr. Lowe, later, furnished the report, as follows:

"The recent meeting was one of the most successful on record, the attendance was large, the interest in the meetings well sustained, and the social features most enjoyable. The standing committees presented excellent reports. The Membership Committee reported 136 new members. The report of the Committee on Trade Interest and that on Adulterations were especially noteworthy, as was also that of the Committee to Draft Antinarcotic Laws and the Committee on Legislation.

"The State Pharmaceutical Examining Board, through its Secretary, L. L. Walton, presented a most complete and satisfactory report of the work done by the Board. The Vice-President of the Board, Christopher Koch, reported the efforts made to stop the cocaine and morphine traffic.



"The prize of \$20.00 for the best paper read at the previous meeting was awarded to Dr. F. E. Stewart, for his paper entitled 'The Copyright, Patent, and Trade-Mark Question.' A touching memorial session was held for the late Mahlon N. Kline. Several of the members voiced their high esteem of his character.

"Affiliation with the N. A. R. D. was maintained, but the appropriation was cut down in amount.

"The social features were, as usual, of a very enjoyable character.

"The only criticism which can be fairly made was the lack of sufficient time given to the reading of papers and queries. Quite a number of papers were read by title. The discussions on those read were very interesting and profitable. Professor Charles H. LaWall was elected President for the ensuing year. The next meeting will be held at Bedford Springs, June 20-22, 1911."

#### ABSTRACTS FROM THE MINUTES OF THE BOARD OF TRUSTEES.

*June 15.*—Fifteen members present.

The Committee on Accounts and Audit reported that they had examined the accounts of the Treasurer, Registrar, and Committee on Publication and found them correct.

The Committee on Instruction presented a supplemental report recommending the appointment of Messrs. Cliffe, Remington, and Kraemer as a Subcommittee on Athletics. The Committee also reported that Professor Moerk had divided the third year class into two sections, arranging them alphabetically, which would prevent considerable annoyance. Owing to increasing work in the Chemical Laboratory, additional assistance was arranged for; and it was recommended that a Department of Physical Culture be organized with William Schleif, Ph.G., M.D., as medical examiner and W. Ward Beam as instructor. The recommendations of the Committee were approved.

The Wiegand Scholarship Fund was reported to be available, and that one student would be named for the session of 1910-11.

The Committee on Announcement reported that Bulletin No. 4, Vol. 2, was in the hands of the printer and would be issued early in July. The Committee asked the opinion of the Board as to the advisability of issuing an edition of the Bulletin in Spanish. The suggestion was received with favor, and the Committee was authorized to prepare a Spanish edition.

The Board unanimously passed a resolution of thanks to be tendered his Excellency, Edwin S. Stuart, Governor of Pennsylvania, for the able and interesting address which he delivered at the Commencement exercises held in the Academy of Music on Thursday evening, May 26. A resolution of thanks was also extended to the Rev. Llewellyn Caley for the services which he rendered upon the same occasion. In appreciation of the very able baccalaureate sermon delivered Sunday afternoon, May 22, by the Rev. David M. Steele, to the graduating class in attendance at the Church of St. Luke and the Epiphany, Thirteenth Street below Spruce, a unanimous vote of thanks was extended Rev. Mr. Steele.

A vote of thanks was extended to Miss Mary Dobbins for the presentation to the College of a picture of the Old Physic Garden of the Society of Apothecaries at Chelsea, England (1750). The picture was much appreciated, and will prove a valuable addition to the collection of the College.

C. A. WEIDEMANN, M.D.,  
Recording Secretary.

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#### NOTES AND NEWS.

COMMITTEE OF REVISION.—The vacancy in the Committee of Revision of the U. S. Pharmacopœia caused by the resignation of Professor Edward Kremers has been filled by the election of Professor Solomon Solis Cohen, of Jefferson Medical College, Philadelphia.

INTERNATIONAL EXHIBITION AWARD.—The exhibit of the Wellcome Chemical Research Laboratories at the International Exhibition at Brussels, which, unfortunately, was completely destroyed by fire in August last, has been awarded three grand prizes (Grand Prix) and one gold medal; and for an exhibit at the Japan-British Exhibition held in London during the past summer, one grand prize was also received. When one reflects upon the large number of researches carried on in these laboratories, and as seen in the numerous scientific papers published under the direction of the director, Dr. Frederick B. Power, we are quite prepared to learn of the announcement of these awards.

PHARMACEUTICAL MEETING.—At the first of the series of pharmaceutical meetings for 1910-1911, held on October 13, Dr. E. R. Larned, Special Lecturer on Serum Therapy, Physiological Standardization and Chemical Testing of Drugs of the University of Buffalo, and Director of the Laboratories of Experimental Medicine, Parke, Davis and Co., delivered a lecture on "Serum Therapy, the Prevention of Smallpox and Opsonic Therapy," which was illustrated with a large number of lantern slides. An abstract of this valuable lecture will be published in an early issue of this JOURNAL.





PROF. CARL S. N. HALLBERG  
1856-1910.



# THE AMERICAN JOURNAL OF PHARMACY

DECEMBER, 1910

CARL S. N. HALLBERG.\*

Carl Svanté Nicanor Hallberg was born in Sweden, October 13, 1856, in the city of Helsingborg, on the Sound, directly opposite the Danish city of Elsinore, with its ancient fort, in which was laid the scene of the story of Hamlet. His parents were Carl and Anna (Kohrtz). An extended sketch of his early life will be found in the November *Bulletin* of the American Pharmaceutical Association. He served as an apprentice with the wholesale drug house of M. K. Smith & Co. which had just succeeded Smith & Shoemaker at 243 North Third Street, Mahlon N. Kline and Washington J. Sellers, an uncle of Mr. Sellers, of Altoona, having become partners in the firm. A position was then, fortunately, secured with E. B. Garrigues & Co., Tenth Street and Fairmount Avenue, where, under the direction of Edwin M. Boring, a most thorough training and valuable experience was afforded. This pharmacy was a revelation; no patent medicines in the store proper, no soda-water, nor cigars, everything in the most perfect order. Rows of stock-bottles in the cellar labelled in a bold hand—a master hand, which he then recognized but failed to fully appreciate until years subsequently—that of Professor Maisch, who had been employed in the pharmacy in earlier years.

The summer necessitated a change in situation, with J. O. Eberhard, and again at the opening of the College with A. Nebeker, where he remained until leaving Philadelphia for Chicago in the spring of 1877, having remained in the city after graduating in

\* We acknowledge the courtesy of Prof. W. B. Day, of the University of Illinois School of Pharmacy, in furnishing the data contained in this sketch, as also for the halftone used in the reproduction of the photograph of Professor Hallberg.—EDITOR.

March, 1876, during the great Centennial Exposition. The next great event, the World's Columbian Exposition (1893), was celebrated by his marriage to Therese Bergstrom, formerly a resident of Stockholm, a son being born in 1897.

After two years of practice as clerk with C. F. Hartwig, of Chicago, he engaged in manufacturing pharmacy, associated with C. G. Wheeler originating the saccharated extracts, of which the "abstracts" of the U. S. P., 1880, were the outgrowth.

During 1888 and 1889 he was associated with C. L. Feldkamp, in the practice of pharmacy in Chicago, the firm engaging in manufacturing preparations of the National Formulary and other pharmaceuticals for which it was awarded the gold medal by the American Pharmaceutical Association, at the exposition held in conjunction with the meeting in Detroit, Mich., in 1888.

First contributing to pharmaceutical journals in 1878, he became the editor of the *Druggist*, afterward the *Western Druggist*, in 1882, relinquishing editorial duties in 1890 to accept the position of professor of pharmacy in the Chicago College of Pharmacy, and in 1896 when this college was united with the University of Illinois his appointment was confirmed by the Trustees of the University. This position he retained up to the time of his death. He joined the American Pharmaceutical Association in 1879, the Illinois Pharmaceutical Association in 1881, serving as secretary in 1890-91, and he has been elected honorary member of a number of western State pharmaceutical associations.

A member of the Committee on the National Formulary since its formation in 1886, he has contributed to its three editions. A delegate to the meetings of the Pharmacopœial Conventions held in 1890, 1900 and 1910, he was elected a member of the Committee of Revision by each Convention.

He has contributed a large number of papers to the American Pharmaceutical Association, embracing a great variety of subjects. He was secretary and chairman in 1892 of the Section of Scientific Papers. He was most active on all questions affecting pharmaceutical education and legislation, having instituted the statistical reports to serve as the basis for more thorough and scientific pharmacy laws.

He had been editor of the *Bulletin* of the Association since its first issuance in 1906, and in almost every phase of Association work he has been an active and tireless worker.

Recently he was elected Chairman of the Sub-Committee on Miscellaneous Galenicals of the Revision Committee.

Since 1901 he has been a member of the Council on Pharmacy and Chemistry of the American Medical Association; in fact, we understand that the credit for the origin of the Council was his; and his pharmaceutical knowledge has been of much service to that organization.

He passed away on October 22, 1910. The funeral services were held at his late residence, 4069 Kenmore Avenue, Chicago. Representatives from all the interests with which he was connected were present.

The honorary pallbearers were members of the Chicago Veteran Druggists Association and the A. Ph. A.; the active pallbearers were Professor Hallberg's colleagues of the Faculty of the School of Pharmacy of the University of Illinois.

The funeral services were impressive. President Eberle made a touching and eloquent address. The funeral pieces were beautiful and numerous. Interment was made in Graceland Cemetery in the lot where the remains of the late Albert E. Ebert rest (the lot being a part of the Ebert Legacy to the American Pharmaceutical Association), in recognition of the services of C. S. N. Hallberg to the American Pharmaceutical Association.

In a letter to the editor of this JOURNAL, Prof. W. B. Day, one of his colleagues, says:

"Professor Hallberg was a man of marked personality and unusual ability. He was thoroughly courageous and at all times ready to give battle for his convictions. His honesty was never questioned, and although his friends were sometimes hurt by his intense aggressiveness which occasionally bordered on harshness, yet almost invariably those who had become estranged from him were won back by the frankness, ability, and evident honesty of the man.

"He possessed a wonderful memory, and kept well informed upon all subjects relating to pharmacy. In fact, he was a veritable mine of information on pharmaceutical topics, and was constantly drawn upon by his friends for help in this respect.

"Friends and former students of his frequently sent him difficult prescriptions from all parts of the United States, and often these were written in some foreign language. Only recently a Nebraska pharmacist sent him a prescription which had been filled originally

in Argentina. It was seldom indeed that he failed to decipher these prescriptions and to give the information requested.

"Professor Hallberg exerted a powerful influence over his students, and this influence was entirely for good; especially would he urge these young men to strive for the attainment of pharmaceutical ideals. He was urgent in his advice that they join the leading pharmaceutical organizations, both state and national, and especially would he use every argument to convince them of the need for their joining the American Pharmaceutical Association. He secured more new members for the Chicago Branch than any other officer, although his time was so occupied that he was able to give but very little of it to this cause.

"His labors were most unselfish, and it is not surprising that he left little property. His interment in the Ebert lot was a fitting recognition of the close personal friendship which existed between these two great pharmaceutical leaders and the many attributes which they possessed in common.

"Professor Hallberg's place in the pharmaceutical world will be exceedingly difficult to fill. Few men possess the energy, mental power, and the physical endurance necessary to carry the amount of work that he carried so successfully for many years."

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## INSECTS DESTRUCTIVE TO BOOKS.\*

BY WILLIAM R. REINICK.

Chief of the Department of Public Documents, The Free Library of  
Philadelphia.

Through and through the inspired leaves,  
Ye maggots, make your windings;  
But oh! respect his lordship's taste,  
And spare his golden bindings.

ROBERT BURNS.

I have been investigating the subject, "insects that destroy books," for a number of years; and this paper is simply a summary of a few of the facts that I have discovered and collected. No attempt has been made to make it complete, either as to species of insects, or subject matter under any particular group. These, in a

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\* Copyrighted by the author, 1910.



complete form, with the results of the further experiments now being made to prove the theory advanced, will be published later.

Various insects have been named as the true bookworm. The insect known as the cigarette beetle, *Sitodrepa panicea*, is given as the true bookworm by Prof. L. O. Howard, United States Entomologist; but if the name of "bookworm" is given to the insect which causes the greatest destruction, then this species will have to be placed quite a distance down in the list. Personally, I will not try at the present time to settle the question as to the species which is to be given this doubtful honor.

That a knowledge of the fact that books are destroyed by insects is not of recent acquisition may be gathered from the writings of the ancients.

The earliest reference, according to Austen,<sup>1</sup> was rescued from oblivion by the lad Salmasius, in 1606, when he discovered the manuscripts of the anthology of Cephalus, in the libraries of the Counts Palatine, at Heidelberg. Among the fragments in this collection is one attributed to Evenus, the sophist-poet of Paros, who wrote about 450 B.C.

Aristotle speaks of a "little scorpion-like creature found in books," which was evidently a species of *Acarina* or pseudoscorpions. Horace and Ovid also speak of the bookworm. Pliny, in his "Natural History," has very little to say upon the subject. Martial, who lived in the first, and Lucian, in the second century, A.D., speak of the bookworm, and many other writers mention them; but it was not until 1665, when Hook in his "Micographia," published an account and gave an illustration of the insect, that entomologists were enabled to determine with any accuracy the insect that was named as the cause of the destruction of books. It is impossible from Hook's description to tell what species was meant; but the illustration accompanying the description shows that it must have been a species of *Thysanura* or *Collembola*, commonly known as the silver-fish and spring-tails.

It has been stated that more books and papers are destroyed by small forms of life in one year than by fire and water combined; and, from the facts given by various writers, and the statements made to me in letters by many librarians and others, especially where the libraries are located in the warmer regions, I am positive that

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<sup>1</sup> Bookworms in fact and fancy, *Popular Science Monthly*, 1899, vol. 55.

this statement is true. Those in charge of collections in the temperate regions, whose volumes are not as rapidly destroyed, are apt to doubt the enormous destruction of books each year by practically unseen life.

Again, that this destruction is great enough to cause alarm, is indicated by the number of prizes offered by various bodies for means to prevent this never-ceasing destruction. Prizes were offered by the "Royal Society at Göttingen" in 1774, the "International Library Congress" in 1903, etc., but as yet no satisfactory results have been obtained. I hope before long to be able to present to the world the cause of these ravages and a means of preventing them.

Those who have read articles upon the destruction of books and papers by insects must have noticed that in almost all the papers the author has simply stated that the insects were after the paste used in the binding; and most of the prizes that have been offered from time to time have the same object in view. If the paste is the object of attack, why is it that photographs, which are fastened to the cardboard by means of paste, are not eaten?

Although some of these writers have stated that the bindings were bored or gnawed, a gallery leading from an opening made on the outside towards the interior of the book; that the glazed surface of the paper was eaten off; that in a few cases that portion of the page which had received the impress of the printer's ink only had been eaten, making the page look as though the letters had been cut out with a punch; and again, that a cavity had been found in the interior of the book, without showing by what means the insect was able to obtain access: not one of them, as far as I have been able to find, has reasoned upon the question that there might be other causes for these ravages of the insects upon books besides the hackneyed phrase, "that they are after the paste used in the binding, in order to obtain the starch contained in it."

Having read hundreds of articles and notes upon this subject, and having had the pleasure, from my standpoint—but not that of the librarian, of examining many hundreds of volumes of ancient and recent date of publication, with bindings made of different leathers, paper made of rag, wood, and other materials, my attention was before long attracted by the fact, that in the great majority of books examined no attempt was made by the insects to eat the paste used in the binding, and also by the many cases in which a

cavity or cavities were found in the interior of the volume without showing the means by which the insects obtained access thereto.

Looking at the various ways in which books were ravaged, and knowing from my own studies and observations in entomology that the insects have wonderful instinctive powers, which in a number of cases could very easily be classed as intelligence, I have come to the conclusion that there must be other reasons besides the desire for paste, to cause these various depredations, and I have asked myself this question: "As we know that the dog and cat, when sick, look for certain herbs, grasses, and putrid animal matter, being directed by their instinct to that substance which contains the vegetable and mineral matter which is best suited for the particular ailment from which they are suffering at that particular time, may not the insect, with an instinct as great if not greater, have use for them for the same purpose?" It seems to me, that the lower we go in the scale of life, according to the classification of the systematists, the more wonderful are the instinctive faculties of the small forms of life, and that if a classification was made according to instinctive faculties, it is a question whether the ants would not outrank the animals by many degrees.

The new school of medicine, in departing from the system of the old, that is, that in which Hahnemann in following Paracelsus claimed that certain symptoms in human beings required mineral agencies and vegetable compounds in potencies equivalent to the complaint, neglected to study the power of drugs, and results not anticipated frequently occur, caused by not using judgment in the quantity of the dose given. Those interested in finding means for destroying life that is destructive, should use the means as those advocated by Hahnemann in their researches.

Starting upon this theory which I contend will be found to be true, when biologists, physicists and entomologists have searched more deeply into the evolution of the lower forms of life, I divided the books into classes according to that portion which was damaged, and will describe some of the most important and name a few of the insects which attack that particular group.

PASTE EATERS.—Science has proved beyond doubt or question that there can be no destruction of matter, only a change of form. If there is no destruction of matter, then we have a demonstration of the theory of the worm or larva having been attracted to the paste used in the binding of the books. In the agricultural kingdom we

find that rye, wheat, and the various other varieties of grain are constantly being damaged by the work of different species of insects. These insects and other small life live upon the exudations of plant life, and the human body is also giving off exudations in the form of perspiration which is also a source of nourishment to many forms of life.

We will take rye and wheat, which are principally used in paste making, as an example. The whole grain is taken to the mill, husked and ground, and prepared by various processes for the sustenance of the human family. After all the processes of the miller have been completed, it is barrelled or bagged and is ready for distribution. In the processes we find that alum has been and is still being used as a whitening agency for the different grains. The flour is taken into the factory apparently pure, clean, and free from all forms of animated life; but in a very short time, especially if it is kept in a compartment that is heated, or in a moist atmosphere, and is left standing some time before being used, life is apparently created in it, a puzzle to all, as to its origin and nature, and stranger still, the first life noticed is always worm life. In this case it is known as the "flour-worm." Mr. James Stone, a flour merchant of Philadelphia, in reply to my questions, stated that they always discovered the worms first, that they were only found in the centre of the barrel, never near the sides, and that the loose flour laying around the floors, of which there always was a quantity, was never found to have worms in it. The lower or coarser grades which are used exclusively for paste were first damaged. The finer grades were more seldom found to be affected. This goes to prove my theory that the life was in the flour before grinding, and that it lay dormant until the proper conditions were produced, such as heat and dampness. The grinding of these grains allows the gases in the air to reach the particles which, to a large extent, were before protected by skin or husk. These gases cause a chemical change to take place, which has been little studied, and this will be found to give food for forms which were heretofore in a dormant condition. Many eggs of the smaller forms of life can hardly be seen, even with a compound microscope. The following are some of the species that may be classed as paste eaters: *Pyralis farinalis*, a moth, and *Tenebroides mauritanicus*, *Silvanus surinamensis*, *Calandra granaria*, and *Tenebrio molitor*, all beetles.

PAPER.—Paper is made from cotton, linen, hemp, rags, and



waste, from chemically prepared woods, from straws, from bark without the wood, from wood not chemically prepared, and many other substances. In a gréat many papers, clay and other minerals are added as fillers. While we are conversant with the various processes used by paper manufacturers, yet very little attention has been given to the real character of life that dwells within the manufactured product in its primoid state. Cotton fly is used for low paper stock, and the little insect that infests the cotton boll, known as the cotton weevil, sends forth its offspring under a different form, yet with all the instincts of itself.

After the paper has passed through certain stages, but not with sufficient intensified heat to destroy the principle of existence, the species evolutionizes into another state or mode of living. In the broader conception of biological truths, ready answers are given to this profound question, *i.e.*, the origin of various forms of life, and the researcher has ready for the querist the proper foundation whereon to build the superstructure of that truth which the arcanum of nature reveals to the desires of the mind of the scientist and physicist. Too little attention has been given to the manuscript notes of scientific workers, often only a line or two of their observations upon the small forms of life. The average scientist thinking it too trivial to notice, often passes over the very observation, which is the key to the puzzle that he has been spending years in trying to solve.

PAPER EATERS; WOOD PULP.—A species of insect, frequently found in libraries, is the *Cimex lectularius*, vulgarly known as the "chinch" or "bed-bug." Its natural instinct leads it to wood on account of certain poisons in the form of acids contained therein, and certain nourishments which are of a poisonous character to the human being, but beneficial and necessary to insects and worm life. Where paper has been manufactured from wood pulp, containing the particular acids or poisons which the "bed-bug" requires, there you will find the insect with all its instinctive faculties. Why do they live and thrive under wall paper? Many wall papers, some of which are known to be a cause of illness to mankind, have large quantities of arsenic, cochineal, and paris green in them. This mineral compound, being changed by the continual variation of temperature going on in the room, is sufficient to change the natural character of the paper, and also the habits of the bugs, who are thus able to obtain nourishment from the back of the paper.

Among this group may be found the following beetles: *Apate capucina*, *Xestobium tessellatum*, and *Lyctus unipunctatus*.

PAPER EATERS; VEGETABLE FIBRES.—In the Aztecan history many of the primitive documents were made from banana skin. These were made to receive the imprint, just the same as paper is manufactured for printing to-day. A sample of this paper was placed in a perfectly sealed case, and a scholar wishing to refer to it one day, upon going to the case containing the writing, was astonished to find that all the paper had been entirely destroyed, although the case was still impervious to any attack made from the outside. This demonstrates how long life may be prolonged, in the sense of the insects being placed away from their natural surroundings, continuing the life cycle whenever the proper conditions are given.

*Trichophaga tapetzella*, *Tinea pellionella*, *Tineola biselliella*, and *Plodia interpunctella* are a few of the moths that bore into paper in order to obtain access to the fibres.

PAPER EATERS; MINERAL FILLERS.—This group includes papers where quantities of clay and other mineral substances have been used as fillers. For an illustration we will take the character and life habits of the *Termites*, or white ants, which are in a measure destructful to material utilized in the manufacture of paper. The alluvial deposits are natural to the white ant, consequently, when clay is used in the manufacture of paper, the instinct in the ant leads it to feed upon that which is natural to it, especially if the books have been kept in a place where it is damp. The lower organic life is, but in a measure, an evolution that is manifested in the higher and more complex forms of life. In the mountainous region of North Carolina is found a collection of people who eat large quantities of clay which is found there in abundance. These creatures, the whites being designated as "poor white trash," and the negroes as the "blue-gummed negroes," are addicted to the habit of clay eating, and nearly all are veritable living skeletons. The eyes and gums of the whites have a reddish hue, and their skins become a dirty yellow; and the gums and skins of the negroes take on a bluish hue. This clay contains arsenic, and, instead of clay eaters, they might more properly be called arsenic eaters. The supply of clay for daily use is provided with more energy and precision than food. This clay poisons the saliva exuding from the glands of the mouth, and also from the base of the teeth, and makes their bite probably poisonous.

And so we see the special laws of nature by which forms of low life live, actuated by the first principles of their instinct to return to their primitive mode of feeding; that is, the life that is generated from the botanical kingdom, much in sympathy with the facts established by Dr. Hahnemann, which verifies the principle that like attracts like.

*Monorium pharonis*, or red ants, *Termites*, or white ants, are found destroying paper that has clay in its composition. The first named is also fond of saccharine that is found in wood fibre.

PAPER EATERS; ANIMAL FIBRE, PARCHMENT.—Insects, such as roaches, which destroy parchment, are after the oils and fats which are used in their preparation; for however carefully the parchment may be prepared, there is always a certain amount of oil and grease left in it. These oils are obtained from the plants, minerals, and animals of the earth, which the roaches have always been used to; therefore, when placed in a location away from their natural food supply, their instinct compels them to seek those books which have the foods, etc., in their composition to which the roaches formerly had access. After the processes of the manufacture of the paper have been completed and it is ready for the printer, another transitional change is nigh, due to the chemicalization of the inks that are used.

Parchment is especially eaten by the roaches, *Periplaneta americana*, and *Ectobia germanica*, the crickets, *Gryllus assimilis*, and some species of *Coleoptera*, or beetles.

SKIN BINDINGS.—Bindings made of skin always have a certain amount of oily or gelatinous substances in them, even though they may seem perfectly dry to the observer, and these bindings are subject to the ravages of the insects that in their natural state go after substances containing oils and greases. Leather that is perfect in its external appearance, under degrees of dampness will expand, and under degrees of heat will contract. The oil is hidden at the bottom, and does not come to the surface until pressed out by expansion caused by dampness. The skins contain the same elements in the dead state as in the living, and the bindings will be attacked by the same forms of life that lived upon the live animals, because they can still find the mineral poisons and the alluvial substances that were part of their natural food supply. Leather bindings are also subject to the depredations of insects and worms which are partly after the oils, acids, and fats which are in the skin, as well as from the new

life that has been conveyed to it by the uncleanness in preparing the leather, not including the hundreds of substances, many of them poisons, especially tannic acid, used by the tanners for tanning purposes, which are also attractive to other species of insects. And just as the animals which eat the plants containing various chemical elements thus become impregnated with acids, so will the insects living upon animals and plants be found to have acids in their compositions.

The leather is destroyed by a number of species of beetles, such as *Lasioderma serricorne*, *Attagenus piceus*, *Dermestes lardarius*, and *Anthrenus scrophulariæ*.

WOOD BINDINGS.—The beetles, *Anobium hirtum* and *Ptilinus serricornis*, are found making galleries in the wooden covers of books.

POISONS USED, MINERAL.—We have in the minerals of the earth many poisons, one of which, arsenic, is of especial interest, as it has been the established rule of the wall paper manufacturers to use it in large quantities; and this poison is one that attracts various species of insects on account of its medicinal value. Just as human beings take poisons in proportionate ratio to the needs of their systems, and especially arsenic, for their health, so do the insects and lower forms of life, which have an instinct beyond the ordinary comprehension, need it; and they find it in the wall papers and colored illustrations printed on the bindings and in books. Where sulphur is used, other species will be attracted, and so on with the various poisons which are used in the arts. The "bed-bug" also finds food in the poisons used, such as arsenic, Paris green, etc. The idea that this insect is found only where uncleanness prevails has long since been rejected, as it is constantly found where absolute cleanliness prevails.

Flies will cling to wall paper, especially in damp weather. This is due to the moisture in the atmosphere causing the poisons in the paper, which flies are primarily after, to become soft enough for them to eat.

GASES; FROM HEAT.—It is accepted as a fact by scientists to-day that the nature and character of life, in the material sense of evolution, has for its base the heat generated by the physical sun, assisted by the moisture of the atmosphere, and the darkened chambers of the earth, which are necessary in the first stages of all life production. Books in a very dry and warm location will be found to be



subject to attacks of species of *Thysanura* and *Collembola*, which are naturally attracted by heat; and, as heat rises, the books on the top shelves will be found to be the ones damaged by these insects. They are seldom found where it is damp.

The spring-tails, *Lepidocyrtus americanus*, and the silver-fish, *Lepisma saccharina*, come under this group.

GASES; POISONOUS, ETC., COMBINED.—The tree, from which is made the wood pulp used in the manufacture of paper, has its roots shooting down into the bowels of the earth, and its branches and leaves reaching up into the heavens. The roots are fed by a varied combination of elements, mineral, gaseous, and vegetable, and these elements, taken in by the roots, are by a wonderful system of arteries carried into every portion of the tree, and insects are thus able to get all elements that are necessary for them to sustain life. The pores of the skin are the health holes of the body, and in a sore, unless it is sterilized, life is bound to start, and that first life again is worm life, no matter how carefully the wound is protected on the outside. If a microscope was used, the body would be found to be covered with animated matter. The insects, preying upon animal life, are after the poisons exuded by the blood and skin.

OMNIVOROUS.—Among the insects which can find food in all portions of the books may be mentioned the beetles, *Sitodrepa panicea* and *Tribolium confusum*.

CARNIVOROUS.—The following are some of the forms of life found preying upon insects found in libraries, the centipede, *Scutigera forceps*, pseudoscorpions, *Bryobia pratensis* and *Tryoglyphus longior*. I believe that investigation will show that the two last species are injurious to books.

RESEARCHES.—Some of the statements here made seem radical, but when it is considered how little is known of the life habits of the lower forms of life, on the one hand, and the facts given by the few life histories that are known, on the other, it does not appear to me unreasonable to place this theory before the public. Especially so, as my own experiments are showing results entirely different from anything hitherto published.

It is known that the eggs of the insects under adverse conditions will stay fertile for long periods of time; that the eggs will also stand a very high or low temperature; and, on account of the toughness of their skin or shell, are also able to stand a great deal of handling and pressure without being crushed or broken. At an

institution with which I was officially connected for a number of years, a lot of mosquito eggs were received from Cuba. These eggs had been attached to a piece of rough blotting paper, and sent to us through the mails. Upon receiving them, thinking that they had been ruined by the rough handling and pressure that they must have received in transit, the blotting paper was thrown aside and allowed to lay exposed to the dust of the atmosphere and the rays of the sun for many months. One day, in a spirit of fun, some one threw the blotting paper into some water, and, to the surprise of all, in a very short time, the larvæ were swimming around as though nothing had ever happened to them.

All plants, vegetables, trees, etc., have certain combinations of chemical elements which are only found in them, as is known from chemical analyses which have been made of material from them, and each of these have certain forms of life which live upon them, and whenever any of these trees, etc., are used in the manufacture of paper and preparation of leathers, eggs of the different species are most likely to be found incorporated in the material; hibernating, as it were, until the proper conditions through heat or dampness come about, giving life to the germ within, and in a very short time the little worm is enjoying life, although being evolved perhaps, later than nature intended it to be.

Again, wandering insects come into the library, and their instinct tells them what books contain the particular food or medicine for which they are seeking. These little insects pass through their various states of evolution, with long periods of life, which are unknown to the finite mind of man as to the exactness of the length of their lives, and are always evolving up to a point of superior consciousness. We must give credit to the entomologists for their researches as to the laying of the eggs of the winged insects, that in time, by the active energies of the physical universe, produce life which becomes expressive, by a process of incubation which has been very little considered. These various illustrations are exhibited to express the nature and character of that which has been infectious to the libraries of the world. While many of them will seek for the paste, it is not always that which attracts them. They are also attracted by the mineral and vegetable substances found in books.

DISEASE CARRIERS.—Just as diseases are carried by flies, the seeds of plants by birds and the winds, so are contagious diseases carried to new locations by books and papers. Flies coming from

putrid matter, or from a person suffering from a contagious disease, by depositing disease germs on books provide the means, if given the proper conditions, of spreading these diseases to a locality where they were unknown before, not to mention the possibilities of fleas, germs, and bacteria. From my knowledge of the ability of bacteria to attach themselves to paper, I am positive that future research will show that books and papers have been the means of spreading many cases of disease. The question of doing away with bank notes has been agitated for years, on account of the disease germs and bacteria carried on them, absorbed from the unclean hands which handle them. A letter received by me from the United States Bureau of Animal Industry states that, "Several years ago, however, at the request of a Representative in Congress, an examination was made by this bureau of a one-dollar Treasury note with the view of determining the number of organisms thereon. The note used for the investigation was obtained on February 3, 1904, from the U. S. Treasury, having been withdrawn on that date from circulation. It belonged to Series 1890, and hence had been in circulation thirteen years. While the note looked very old and quite soiled, one often receives notes of even worse appearance in ordinary business transactions. .

"The note in question was subjected to the ordinary laboratory manipulations for determining the number of micro-organisms upon it which were capable of vegetation and development, and as a result of this examination it was found that there were 13,518,000 living micro-organisms present on this note. These consisted principally of the organisms popularly known as bacteria and fungi." Uncleanliness is more to blame than the paste in the books for insects found destroying them.

The fleas, *Pulex serraticeps*, and other species, and the *Acarina*, or pseudoscorpions, are also capable of carrying disease germs.

REMEDIES.—As far as the destruction of these insects by poison is concerned, they are practically worthless, because, whenever the poison is used to destroy one insect it will attract other insects that have need for that poison. Uncleanliness of the human family also helps to supply the needs of the bookworm. Men and women do not give the proper consideration to their hands, going from the dining-room into the library, either public or private. Nature, by its process under the great infinite power, has supplied the skin of the human body with scales and pores, and these, acting upon

their functional duties, are constantly discarding that which the body in a healthful state does not want. In perspiration, which is moisture, there is thrown from the pores of the skin a combination of mineral and vegetable acids, and this may all be summed up in the word "dirt." This combination, or dirt, contains food for a number of species of insects. When the hands which are soiled are laid on clean paper, some of the matter attached to the hands will be left upon the paper, in this way producing food for insects. We say this, because man from a material stand-point has his grosser body made of matter, and matter in a concrete form is made of the dust of the earth. Cleanliness in the handling of papers, books, and documents will be of more value than all the poisons combined. Let common-sense prevail, make sanitary rules in the home and in the public library an enforced rule, and it will lessen and arrest the rapid growth of the little insects which feed upon our silent friends of so much value to us, besides eliminating the possibilities of contagious diseases. The library of the future will be found to contain laboratories where every one wishing to make use of the books in the collection will first have to thoroughly cleanse his or her hands. This is a subject which should be considered in the near future by the bacteriologist, as well as the entomologist, biologist, and general visitors to the halls of learning.

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## SHALL WE HAVE A PROFESSION OF PHARMACY?

BY F. E. STEWART, PH.G., M.D.

(*Concluded from p. 534.*)

There is some truth in this claim, but if the physicians and pharmacists of this country had given the public a square deal regarding materia medica products, the present conditions need never have arisen. Unfortunately, the medical schools have neglected to properly teach materia medica, while the retail druggists have carried on a proprietary medicine business of their own on a smaller scale, to which are equally applicable the very objections they now urge against the manufacturing houses. But a reaction has occurred. The worm has turned. And the pure food and drug laws, instead of resulting from co-operative effort on the part of the medical profession and the retail druggists to reform conditions, are largely due to public resentment of the deplorable conditions mentioned. This reform should have come from the medical and pharmacal



press, not from *Collier's Weekly*, the *Ladies' Home Journal*, and other non-professional publications.

On the other hand, all must concede that centralization is the tendency of the day in all lines, and the great manufacturing houses have come to stay. Nearly every manufactured article is now produced on a large scale by great plants, with which individual houses working on a small scale cannot hope to compete, and as standardization of all products becomes more prevalent the small manufacturer will have still less chance of success. The cost of standardizing one pound of steel as to carbon content is as great as the cost of standardizing a ton, therefore standardization work cannot be economically conducted except in relation to large outputs, and the same principle applies to materia medica products.

This evolutionary process, due to economic conditions and representing advance in civilization, is by no means completed. Whether or not it will end in socialism remains to be seen. The socialization of medical and pharmacal practice has its advocates, but this phase of the subject is outside the limits of my lecture.

#### THE RETAIL DRUGGIST AS A MANUFACTURER.

Under a professional system, with its common standards and freedom from monopoly, all retail druggists have equal chances as manufacturers, while under the proprietary system, with its monopoly and misleading advertisements, the advantage is on the side of the manufacturers of nostrums, therefore, as a matter of self-interest, the retail druggists should favor the ideal of professional pharmacology. As a class, however, they oppose legislation tending to limit the nostrum business, possibly because each druggist dreams of himself becoming a nostrum king.

Many prescriptions call for ready-made preparations of various kinds, which are now supplied by the manufacturing houses in the form of sugar-coated and gelatine-coated pills, tablets, filled capsules, etc. Druggists engaged in the U.S.P. and N.F. propaganda hope that doctors will discontinue the use of such ready-made products and return to prescription writing, but the tendency away from polypharmacy toward the more scientific use of drugs is as unfavorable to the polypharmacy extemporaneous prescription as to the ready-made polypharmacy prescription.

Progress in pharmacotherapy is along the lines of standardized

materia medica products, and future standardization will include pharmacognosy, pharmaceutical assaying, and pharmacodynamic tests on animals. This is expensive, and must be done on a large scale.

#### WHAT IS THE USE OF PHARMACOLOGIC EDUCATION?

The answer to this question is frequently pessimistic, but my personal answer is optimistic. I believe the future outlook for drug therapeutics is better. Never before has there been greater need for a profession of pharmacology. The members of the profession will naturally specialize. Most of the research work will be done by those engaged in government laboratories and in teaching, although those employed by the large manufacturing houses will conduct original investigations on a smaller scale. Those engaged in the retail drug business will be learned in pharmacologic science, and will occupy the positions of experts regarding the preparation of drugs and their application as remedial agents. They will be manufacturers as far as their facilities permit, or else hold stock in some large manufacturing house, doing all in their power to promote its advancement.

This, at least, seems to be the tendency of things. And this is for the best interests of the public, as it will place the practice of the pharmacologic arts under the control of the pharmacologic profession, where it properly belongs.

#### PHARMACY LAWS.

It is evident that enforcement of the professional ideal of pharmacologic practice under present conditions will place professional pharmacists and manufacturers at a disadvantage in competition with commercial druggists and manufacturers of the so-called "proprietary" medicines. "Professionalism" requires that new products be surrendered for the general good and that all members of the profession be taught how to make and use them. "Commercialism" means the monopoly of new products by individual manufacturers, firms, or corporations, and their introduction to commerce by advertising.

The anomalous conditions of law in this country, by which manufacturing houses are exempted from the operation of both medical and pharmacal laws, permit any person, however ignorant, to set up as a manufacturer and thereby practise pharmacy and therapy

at wholesale without license, to the detriment of the public health. This is one of the abuses for the pharmacologic profession to remedy, and the way has been pointed out by the U. S. Supreme Court in the previously mentioned decision in the Syrup of Figs case. Manufacturing houses should be licensed as are individual pharmacists and physicians.

#### COPYRIGHT, PATENTS, AND TRADEMARKS.

Contrary to common opinion, names of medicines cannot be copyrighted, as they cannot be privately owned by any one. This statement can be verified by addressing the Librarian of Congress. It is an axiom of law that the name of an article of commerce cannot be a trademark, for it cannot at the same time perform the functions of an appellative to distinguish an article from other articles of commerce and a trademark to distinguish a brand from other brands of the same article.

I cannot here repeat all that I said on this subject in my lecture, but I would refer you to the following authorities: the chapter on "Copyright" in the *Encyclopædia Britannica*; Browne on "Trademarks"; Kerley's "The Law of Trademarks"; "Report of the Commissioners Appointed to Revise the Patent and Trademark Laws under Act of Congress Approved June 4, 1888," known as "Senate Document No. 20."

The medical profession is standing between two opinions regarding patents on *materia medica*. One side takes the position assumed by Lord Camden in his celebrated speech on the subject of copyright, when he said: "Glory is the reward of science, and those who deserve it scorn all meaner views."

Those who believe in the patenting of *materia medica* products agree with the statement of Terrill in his "Treatise on Patent Laws." According to this authority, "The theory upon which the laws rest is that it is to the interest of the community that persons should be induced to devote their time, energies, and resources to original investigation for the furtherance of science, the arts, and manufactures. This was recognized from the earliest periods which can pretend to be described as civilized. It is to the advantage of the whole community that authors and inventors should be rewarded, and no measure of reward can be conceived more just or equitable, and bearing a closer relation to the benefit conferred by the par-

ticular individual, than to grant him the sole right to his writing or discovery for a limited period of time."

Scientists in every line take the position that "Glory is the reward of science," and refuse to recognize as a scientist any person who attempts to monopolize the results of his observations or discoveries. It is said that the true scientist works for pure science, not for the application of science to practical purposes, and that if the medical profession wishes to be a truly scientific body, physicians must not only refrain from patenting their inventions and discoveries, but refrain from commerce in *materia medica* inventions and discoveries.

The professional ideal of the vocation is represented by a class of pharmacists who believe, with me, that those engaged in the practice of the pharmacologic arts should be supported by commerce in *materia medica* products, but that such commerce should be conducted as a professional (not commercial) vocation.

Carried to a logical conclusion, strict enforcement of the scientific ideal would exclude authors of medical books who take advantage of copyright law to secure monopolies of the products of their brains. The copyright law has been found necessary in order to protect capital engaged in the business of publishing medical books; and, without danger to science, the patent law can be applied to the protection of the *materia medica* supply business. The patenting of processes and apparatus for manufacturing products promotes progress in pharmacologic science and arts so long as the patents do not cover the products made thereby. If the sale of the products themselves is monopolized, then the tendency is to force them on the market by misleading advertisements; and, as the errors of commercial exploitation cannot be corrected by impartial discussion, owing to the influence exerted by the manufacturers of controlled products upon the entire press of the country, medical, secular, and religious, the monopoly is disastrous in its effects upon pharmacologic science and practice.

#### THE INTRODUCTION OF NEW BRANDS OF MATERIA MEDICA PRODUCTS TO COMMERCE.

Introducing new products to science differs greatly from introducing new brands of manufacture to commerce; the former requires scientific methods, the latter, commercial ones. But it should be remembered that "Commercialism is not a word in good repute in



connection with the practice of medicine." And this includes pharmacy or the manufacturing of medicines for therapeutic use. The making of money is the mainspring of commerce, and while money-making is not wrong, *per se*, medicine (including pharmacy) has a higher and a nobler aim. If it be not so, our widely uttered claims of being a liberal profession are false, and a large proportion of what we may call the non-scientific part of medical literature (including most addresses to graduating classes in medicine and pharmacy and to societies) is the veriest talking for effect.

#### CONCLUSION.

Shall we have a profession of pharmacology? Yes. But the scope and title of that profession should be enlarged to include the co-operative practice of the pharmacologic arts by physicians, pharmacists, physiologists, botanists, chemists, and all others engaged in investigating and classifying the *materia medica*, and in selecting, preparing, preserving, compounding, and dispensing drugs, and in applying them to the treatment of the sick.

How shall we have a profession of pharmacology? That question cannot be answered in a paragraph or page. Only by complete study of the subject, along the lines I have mapped out, can the answer be ascertained.

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### PROGRESS IN PHARMACY.

By M. I. WILBERT, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

The leading topic for discussion, in medical circles at least, is the possible influence of the report of the Carnegie Foundation on the advancement of medical education, and the really serious attempts that are being made by medical schools generally to raise their requirements for admission as well as improve on their facilities for teaching.

*Medical Education.*—An interesting illustration of the possibilities is evidenced by an article by Henry S. Pritchett, president of the Carnegie Foundation for the Advancement of Teaching, in a recent number of *The Outlook*, on how to study medicine.

He refers more particularly to the fact that the art or science of medicine has been practically revolutionized during the past twenty years and that its practice to-day rests on certain fundamental sciences which were scarcely known thirty years ago, and then points out very clearly that sectarianism no longer has any reasonable cause from existence. The article is commented on editorially in the *Journal of the American Medical Association* (1910, v. 55, p. 1292).

*Medical Education in the United States.*—The educational number of the *Journal of the American Medical Association* (August 20, 1910) contains brief descriptions of the medical colleges in the United States and Canada that are legally chartered to teach medicine. Also enumerates the foreign medical colleges and discusses educational standards abroad and at home. An editorial in commenting on the report points out that the total number of medical students in the United States for the year ending June 30, 1910, was 21,526, a decrease of 619 from the previous year and a decrease of 1076 from 1908. A rather significant indication is the fact that the total number of graduates from the so-called sectarian schools has decreased annually during the past ten years.

*Meeting of the American Medical Association.*—The Board of Trustees of the American Medical Association have decided on June 27, 1911, as the date for the opening of the next session of the American Medical Association, in Los Angeles. This date, which is later than usual, was chosen so as not to interfere with the men connected with medical colleges and was also thought to be more generally convenient for those who desire to take advantage of this occasion for a vacation (*J. Am. Med. Ass.*, 1910, v. 55, p. 1558).

*Pharmaceutical Education.*—Wilhelm Bodemann, in commenting on the Richmond meeting of the American Pharmaceutical Association, expresses the opinion that the one thing that impressed him most has been mentioned least. He refers here to the formal call on the "Carnegie Foundation" to report on the pharmacy schools of the country much in the same way that they had reported on medical schools (*Pacific Pharmacist*, 1910, v. 4, p. 187).

*C. S. N. Hallberg.*—The death of Prof. Hallberg brings with it a serious setback to pharmaceutical education in these United States. For many years he was one of the foremost champions

for advancement in matters pharmaceutic and, though not always right, he labored and fought according to his light, and this, it must be admitted by all, was kept bright by closely following the medical and pharmaceutical literature of the day. His incentive and co-operation will be missed in many fields, but in none so acutely as in the frequently fallow field of pharmaceutical education.

*Berlin Pharmaceutical Institute.*—A news note announces the publication of an attractive volume commemorative of the centenary of the University of Berlin. The book is entitled "Das Pharmaceutische Institut der Universität Berlin," and is written by Professor Dr. Hermann Thoms, Director of the Institute. It contains an account of the development of pharmaceutical education at the University of Berlin since its foundation in 1810, and a detailed description of the buildings now in use (*Pharm. J. (Lond.)*, 1910, v. 85, p. 487).

*International Congress of Pharmacy.*—The International Congress of Pharmacy, held in Brussels, September 1 to 6, 1910, promises to have a potential influence on the progress of pharmacy in all of the many countries represented.

The question of the approximation of the several national pharmacopœias is one that is of great importance and received due consideration, and the communication presented by Dr. Schamelhout on the unification of analytical methods promises to be of service in correlating the standards and the tests included in the several pharmacopœias.

*Nomenclature.*—It is unfortunate indeed that the International Congress of Pharmacy paid little or no attention to the possibility of developing an international nomenclature for widely used medicaments. A recent article in *Science* (October 28, 1910, p. 594) in commenting on the work done in this connection by the Brussels Botanical Congress, and by the International Congress of Zoölogists, which met this year at Gratz, says: "The fact that the problems of nomenclature have assumed sufficient importance to be considered by international congresses should sustain our hope for further progress, especially when we recognize that such matters are subject to the general laws of evolution and education and that perfection cannot be attained at a single bound."

*Commercialism in Pharmacy Abroad.*—An editorial in the *Pharmaceutical Journal* points out that the proceedings of the International Congress of Pharmacy appear to indicate that the com-

mercial element has evidently invaded the pharmacies of our Continental *confrères* to a most unfortunate extent in recent years, and, like English pharmacists, they are desirous of having as interest on their capital, as pay for their labor, as indemnity against bad stock, and as an honorarium for the use of their diploma, some profit on the articles which they sell (*Pharm. J. (Lond.)*, 1910, v. 85, p. 361).

*International Pharmaceutical Federation.*—One of the more important actions of the International Pharmaceutical Congress, held at Brussels, was the adoption of a resolution, proposed by the delegates of the Dutch Association for the Promotion of Pharmacy, which provides for the foundation of an International Pharmaceutical Federation, with headquarters at The Hague. The object of this federation will be the promotion of pharmacy as a science and as a trade, and it is to consist of delegates representing the various affiliated societies.

As pointed out in a recent editorial in the *Pharmaceutical Journal*, London (1910, v. 85, p. 435), the laws and customs governing the practice of pharmacy on the Continent differ fundamentally from those in force in English speaking countries and the deliberations on the business side of the occupation while interesting are of but indirect value to pharmacists either in Great Britain or the United States, so that the benefit to be derived from international co-operation is limited indeed.

*National Department of Public Health.*—The need for developing a more efficient organization for the protection of the health of our people is still uppermost in the minds of thoughtful citizens and has been given considerable space in the pages of medical and pharmaceutical journals.

Among others, Geo. B. Young discusses the nature of the problems involved in the proposed enlarged national public health organization and outlines a plan with reasons for adopting the divisions as proposed. An editorial in commenting on this paper points out that it offers a tangible basis for discussion and can be taken as a starting point for actual constructive efforts; also that the problem of unifying all of the present health work under one general head is one whose solution should not be attempted without careful study of existing conditions (*J. Am. M. Ass.*, 1910, v. 55, pp. 979-989, 1029).

*Public Health Agitation.*—E. J. Townsend, in discussing



"Science and the Public Service," expresses the belief that as a nation we should do as much to promote the conditions for healthful living among our people as to stimulate the development of our national resources. He points out that every citizen, irrespective of vocation, is vitally concerned with those scientific facts that mean better sanitation, better facilities for overcoming and preventing the spread of infectious diseases, in short, with all that knowledge which will enable us to live better, longer, and happier (*Science*, 1910, v. 32, pp. 609-621).

*National Association of Retail Druggists.*—The Pittsburg Convention of the National Association of Retail Druggists, held September 12-16, 1910, has been characterized as being the most harmonious ever held.

The proceedings throughout evidenced conservatism and the convention will no doubt go far to strengthen the association with the retail druggists of this country.

The opposition of the N. A. R. D. to public health legislation was considerably modified, and, on the recommendation of the Committee on National Legislation, it was resolved that this committee carefully consider proposed legislation and, if necessary, prepare and submit amendments thereto, to the end that in the organization of such department or government division, pharmacy be properly recognized and represented.

*Materia Medica in Medical Colleges and in State Board Examinations.*—The Committee on Materia Medica of the National Confederation of State Medical Examining and Licensing Boards and a similar Committee of the Council on Medical Education of the American Medical Association present a report that is designed to foster a more thorough knowledge of the really important drugs, such as are commonly conceded to be practically indispensable in the general practice of medicine at the present time.

The list contains less than 150 drugs, but includes practically all of the really important substances, and a medical practitioner who is thoroughly familiar with the uses and the limitations of the several substances that are enumerated would be thoroughly well equipped to meet any possible indication or need.

An editorial in commenting on this list points out that the medical student, or even the physician, who tries to gain a thorough knowledge of the ridiculously large and bewildering number of drugs on the market is attempting the impossible. He acquires

real practical knowledge of none. In consequence his knowledge of the action and uses of even the most important drugs is often vague and imperfect (*J. Am. M. Ass.*, 1910, v. 55, pp. 1292, 1302-1303).

*List of Drugs for State Board Examinations.*—Haines and Fantus call attention to a list of drugs devised by the Committee on Pharmacology of the Chicago Medical Society, during the winter of 1908, and adopted by the Illinois State Board of Health as a guide in the elaboration of its examination questions. This list contains approximately 120 drugs and preparations and is practically identical with the list mentioned above (*J. Am. M. Ass.*, 1910, v. 55, p. 1573).

*A Restricted Materia Medica.*—William J. Robinson, in commenting on the proposition advanced by the State Medical Examining and Licensing Boards, advising the restriction of materia medica examinations to a comparatively small number of drugs, asserts that it is certainly better to know 100 drugs well than 1000 badly.

*Pharmacopæial Revision.*—The Pharmacopæial Convention which met in the City of Washington last May is still being actively discussed in local and state organizations and also in current journals. In a recent number of the *Pacific Drug Review* (October, 1910, pp. 16-20) Mr. Peder Jensen presents some thoughts that are well worthy of consideration.

Commenting on the several interests represented at the Convention he says: "Of these the medical interest was perfectly legitimate, commendable, and should receive the recognition and approval of the pharmacists of the United States, for unless the medical men are given an opportunity and right to frame up the contents of the Pharmacopœia to suit every reasonable demand that they might present, we could hardly expect that all the past or coming missionary efforts to induce physicians to use the Pharmacopœia should bear any fruit."

In regard to membership of the General Committee of Revision he says: "I feel personal regret that more medical men were not accepted. I also feel personal regret that the Convention should lower itself to a deliberate piece of trickery in excluding medical representation. The day will come when medical men will have the greater responsibility and a greater claim to the framing of the Pharmacopœia."

Commenting on the nature of the coming Pharmacopœia he says: "The Pharmacopœia that the pharmacists of the United States demand must be one that is so precise in its every direction, so careful in the most minute detail, that any person engaged in the practice of pharmacy will be able to perform each and every operation directed in the work."

*Use of the Pharmacopœia.*—An abstract from the *Lancet* points out that the recognition of the British Pharmacopœia as containing official standards for medicines has tended more and more to make the chemical portions of the book encroach upon the medical portions. In other words there has been a tendency to consider the Pharmacopœia from the analyst's point of view rather than the physician's. The abstract further points out that while it is desirable that drugs intended for other than medical use should reach a certain standard of purity, it would appear that this could be achieved by other means than defining them in a pharmacopœia, and that in the compilation of the Pharmacopœia all considerations should be subordinated to the needs of the medical profession, and as a guide to pharmacists (*Pharm. J. (Lond.)*, 1910, v. 55, p. 323).

*Scope of the Pharmacopœia.*—A. S. Loevenhart, in a discussion on the scope of the Pharmacopœia of the United States, points out that the final decision regarding the scope of the Pharmacopœia was left, by the Convention, in the hands of the General Committee of Revision and that this committee can, if it will, restrict the scope to drugs that are generally recognized as being useful or having therapeutic value (*J. Am. M. Ass.*, 1910, v. 55, p. 1370).

An editorial discussing the scope of the forthcoming Pharmacopœia of the United States points out that considerable restriction and weeding out are desirable. The adoption or rejection of the broad principle of wise restriction will determine whether the book is to be a book of scientific materia medica or merely a book of pharmaceutical formulas and standards; or, in other words, whether the Pharmacopœia is to be revised in the interest of medicine or in the interest of medicines (*J. Am. M. Ass.*, 1910, v. 55, p. 1387).

*Publicity in Connection with Pharmacopœial Revision.*—The revisers of the British Pharmaceutical Codex are giving an unusual amount of publicity to the proposed changes that are to be introduced in that book. For some weeks the *Pharmaceutical Journal* has presented formulas with the request that criticisms

and further suggestions be sent to the Codex Revision Committee.

*Metric System.*—An editorial points out that the movement to introduce the metric system of money and weights and measures into Great Britain is at least making progress and points out that the metric system has been adopted by all civilized countries with the exception of Great Britain, the British Colonies, and the United States. The colonies, as a whole, have consistently advocated the metric system whenever an opportunity offered, but their attitude up to now has been one of expectancy (*Pharm. J. (Lond.)*, 1910, v. 85, p. 412).

*Synthetic Remedies.*—V. Coblenz reviews the recent progress among medicinal synthetics and points out that during the last three years the atmosphere relating to synthetic remedies has been cleared somewhat, through the aid of European State Boards of Health and the Council on Pharmacy and Chemistry of the American Medical Association, who have established a clear distinction between true synthetics, medicinal combinations, and quack nostrums (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 352).

A review of the new remedies included in 15 of the most widely-used pharmacopœias presents some rather interesting information relating to the nomenclature that has been adopted and the recognition accorded to several of the new remedies. The following is an indication of the occurrence of these remedies in the several pharmacopœias:

Antipyrin, phenacetin, salol, and sulfonal.....	15
Guaiacol carbonate .....	13
Dermatol .....	13
Diuretin .....	12
Antipyrin salicylate .....	11
Acid, acetyl-salicylic .....	7
Hexamethylenamine .....	6
Heroin .....	5
Silver proteinate .....	5
Veronal .....	3

(*Pharm. Ztg.*, Berlin, 1910, v. 55, p. 604).

*Pharmacology and the Clinic.*—An editorial calls renewed attention to the fact that clinicians are using drugs more and more on the basis of experimental observation, and points out that a



conservative and sane acceptance of the results of laboratory experimentation will serve to eliminate a tremendous amount of rubbish that has accumulated in the Pharmacopœia (*J. Am. M. Ass.*, 1910, v. 55, p. 781).

*Proprietaries in Italy.*—A. Zambler, in a communication in the *Gazetta degli Ospedali*, voices the general discontent that is being felt in Italy with the way in which proprietary medicines are being advertised. He points out that the third edition of the Italian Pharmacopœia includes a notable display of proprietaries, and that it is the only pharmacopœia in the world that vouchsafes such an effective form of official advertising to the manufacturer of proprietary remedies (*J. Am. M. Ass.*, 1910, v. 55, p. 879).

*Alkaloids.*—H. C. Fuller outlines a method for the separation of cocaine and strychnine and atropine and strychnine when they occur together. The method depends on the ready hydrolysis of cocaine and of atropine, leaving the strychnine to be shaken out with chloroform (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 378).

*Asafetida.*—W. A. Pearson points out that much of the variation regarding the composition of different consignments of asafetida is due to the variation in sampling this drug. He calls attention to the difficulty of collecting representative samples and the need for adopting a more uniform method of collecting samples (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 421).

*Agar-agar.*—Th. Dietzsch calls attention to a form of cut agar-agar that is now available on the European markets. This coarsely comminuted form is thought to be medicinally superior to the ground or powdered substance, but is equally well taken by the patient. In practice the substance is best administered with porridge or oatmeal at breakfast time, in doses of about a tablespoonful (*Pharm. J. (Lond.)*, 1910, v. 85, p. 383).

*Arseno-Benzol and Arsen-Phenol-Amin* are names that are being applied to Ehrlich's "606," the remedy for syphilis and allied diseases that has attracted such wide-spread attention abroad. The remedy will be marketed in this country in the very near future and promises to be one of the most popular new remedies ever introduced.

*Camphenol.*—The chemical laboratory of the American Medical Association reports that examination of camphenol shows that this preparation is but a modification of the well-known camphorated phenol: a portion of the phenol having been replaced by cresol

and the resulting liquid diluted and emulsified with gelatin or some similar substance. The production is said to contain relatively small quantities of the active constituents (*J. Am. M. Ass.*, 1910, v. 55, p. 1662).

*Capsicin*.—E. K. Nelson discusses the detection of comparatively small amounts of capsicum in mixtures by isolating the contained capsin and testing physiologically (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 419).

*Cocaine, Volatility of*.—H. C. Fuller points out that cocaine is volatile at 100° C. and that this fact is important in connection with analytical work and should be noted in the Pharmacopœia (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 426).

*Diaspirin*.—This is described as being succinyl-disalicylic acid; a salicylic acid derivative, produced by the interaction of the two carboxyl groups of succinic acid with the phenolic hydroxyls of two molecules of salicylic acid and the elimination of two molecules of water. Diaspirin is an odorless, and almost tasteless, white, crystalline powder said to melt at about 178° C. It is a dibasic acid which reacts with bases, organic and inorganic, to form salts. The usual dose is 1 gramme three times a day (*J. Am. M. Ass.*, 1910, v. 55, p. 666).

*Digestive Tablets*.—Puckner and Warren discuss the fallacy of using any one of the many combinations of pepsin, pancreatin, diastase, hydrochloric acid, and lactic acid that are offered in the form of compressed tablets. They point out that "shot gun prescriptions" of this type catch the unthinking doctor as well as the self-drugging public who still adhere to the old theories regarding digestive ferments (*J. Am. M. Ass.*, 1910, v. 55, p. 710).

*Ergot*.—Wood and Hofer discuss the pharmacology of ergot and point out that ergot is a stimulant to all the unstriated muscle tissue of the body. They believe that the degree of elevation of blood-pressure affords an accurate criterion of the activity of ergot and that the active principle is an alkaloidal substance which occurs in the drug, probably in chemical union with a resinous body (*Arch. Int. Med.*, 1910, October. *J. Am. M. Ass.*, 1910, v. 55, p. 1681).

*Ferratin*.—Chemically this is known as sodium ferrialbuminate and contains the equivalent of 6 per cent. of metallic iron. Ferratin occurs as a light brown, tasteless powder having a faint odor. It is soluble in weak alkaline aqueous solutions, from which solution it is precipitated by hydrochloric acid. It is given in doses of

0.5 gramme, three or four times a day (*J. Am. M. Ass.*, 1910, v. 55, p. 666).

*Arsenoferratin*.—Sodium arsenoferrialbuminate is an arsenic iron albumin compound, obtained by introducing the element arsenic into the molecule of ferrialbuminic acid. It is said to contain the equivalent of 6 per cent. of metallic iron in organic combination, and the equivalent of 0.06 per cent. of elementary arsenic. Arsenoferratin is a brown, almost odorless and tasteless powder that is easily soluble in dilute alkaline solutions. The dose is 0.5 gramme, three or four times a day (*J. Am. M. Ass.*, 1910, v. 55, p. 666).

*Ginseng*.—A news note announces that Dr. K. Miyake and Mr. Toniye have been sent to this country by the Korean Government to investigate the cultivation and particularly the diseases of ginseng. This drug is considered to be of great importance in Korea and is under a government monopoly. During the past few years there has been a remarkable reduction in the output, due to various diseases similar to those affecting the plant in this country (*Science*, 1910, v. 32, p. 625).

*Hexamethylenamine*.—Molecular combinations of hexamethylenetetramine with guaiacol are being experimented with and promise to be useful additions to guaiacol therapy (*Chem. Tech. Repertorium*, 1910, v. 34, p. 509).

*Hexamethylenamine in Pellagra*.—B. B. Bagby reports unusually satisfactory results from the treatment of a case of pellagra with 15 grain doses of hexamethylenamine, given three times a day, and quotes Beverly R. Tucker as having had equally promising results from the use of the same drug (*J. Am. M. Ass.*, 1910, v. 55, p. 1663).

*Hydrogen Peroxide*.—Linwood A. Brown discusses the determination of free acid in hydrogen peroxide solutions and points out that the U.S.P. test for free acid does not give correct results. He reports a number of experiments and concludes that acetanilid acts the part of a free acid and seriously interferes with securing accurate results. Direct titration in the cold was found to be satisfactory and gives results that are sufficiently accurate for all practical purposes (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 377).

*Hydronaphthol*.—A sample of hydronaphthol examined in the Chemical Laboratory of the American Medical Association had the characteristic appearance, odor, and taste of naphthol and

responded to all of the U.S.P. tests for betanaphthol with the exception of the melting point, which was found to be  $119^{\circ}$  C., in place of  $122^{\circ}$  C., an indication of impurity. The conclusion is reached that hydronaphthol is merely a trade name for betanaphthol (*J. Am. M. Ass.*, 1910, v. 55, p. 878).

*Iron iodobehenate*.—Basic iodobehenate of iron is described as a reddish brown, amorphous, nearly odorless and tasteless powder, containing about 25 per cent. of iodine and 5.6 per cent. of iron. It is insoluble in water and in alcohol, but readily soluble in ether (*Chem.-Tech. Repertorium*, 1910, v. 34, p. 509).

*Kephalose*.—J. R. Hurly reports on the examination of "Kephalose," a French proprietary exploited in the Philippine Islands. The nostrum was found to consist largely of antipyrin and caffeine with a trace of acetanilid and a small percentage each of potassium bromide and sodium carbonate (*J. Am. M. Ass.*, 1910, v. 55, p. 1040).

*Lime*.—L. W. Bahney outlines a method for the rapid estimation of calcium oxide in lime. He points out that the percentage of calcium oxide depends on: 1. The purity of the limestone. 2. The degree of burning temperature and time. 3. The length of time the product has been stored, and whether it has been dry or damp during this period of storage. The method of assay depends on the titration of finely powdered lime suspended in distilled water with oxalic acid, using phenolphthalein as the indicator (*J. Ind. and Eng. Chem.*, 1910, v. 2, p. 407).

*Papaver somniferum* L., M. G. J. M. Kerbosch presents a comprehensive study on the formation and distribution of several of the more important opium alkaloids in different parts of *Papaver somniferum* L. (*Arch. d. Pharmazie*, 1910, v. 248, p. 536).

*Santonica*.—R. Goerlich calls attention to the work by Katz on the determination of santonin in santonica and in preparations of that drug, and outlines a modification of the latter's method (*Apoth. Ztg.* (Berlin), 1910, v. 25, pp. 801, 812).

*Sera*.—An editorial comments on the untoward effects of therapeutic serums and points out that accidents and untoward effects, which fortunately are extremely rare, usually follow a first injection of serum, only a very few instances being reported in which a second injection has caused serious or distressing symptoms. The percentage of fatalities following the injection of serum is



very small; only a fraction of one per cent. suffer from serious ill effects (*J. Am. M. Ass.*, 1910, v. 55, p. 1649).

*Supracapsulin*.—This is the name used for epinephrine by the Cudahy Packing Co., South Omaha, Neb. (*J. Am. M. Ass.*, 1910, v. 55, p. 666).

*Thigenol*.—Solution of sodium sulpho-oleate, Roche, is described as being a solution of the sodium salts of synthetic sulpho-oleic acids, containing 2.85 per cent. of sulphur. Thigenol is a dark brown liquid having a faint sulphurous odor. It is soluble in one or more parts of water, dilute alcohol, glycerin, and in oily or fatty bases. It is used locally and is also administered internally in doses of from 0.2 to 0.6 gramme (*J. Am. M. Ass.*, 1910, v. 55, p. 666).

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### BOOK REVIEWS.

A TEXT-BOOK OF BOTANY AND PHARMACOGNOSY. Intended for the use of students of pharmacy, as a reference book for pharmacists, and as a hand-book for the food and drug analyst. By Henry Kraemer, Ph.B., Ph.D., the Philadelphia College of Pharmacy. Illustrated with over 300 plates, comprising about 2000 figures. Fourth edition, revised and enlarged. Philadelphia and London: J. B. Lippincott Company.

The fourth edition of Professor Henry Kraemer's "Text-Book of Botany and Pharmacognosy" which has just appeared from the press is printed on excellent, heavy paper, with clear, easily readable type, is well bound, and is a fine appearing book. Like its predecessors it is profusely illustrated with half-tone photographs and line drawings. While in former editions the illustrations have been excellent, a number of improvements have been made, so that all seem perfect in every detail. In no other book extant is more care given to every detail.

The work is the most comprehensive now in print, and too much cannot be said in praise of this latest product of Prof. Kraemer's life-work.

The work is divided into four parts. Part I is given to botany and consists of five chapters. Chapter I will be read with interest by every student of botany. The text and illustrations carry one along to a true conception of the evolution in plant life. In Chapter II, roots, stems, fruits, etc., are studied in classes, with reference to their "Outer Morphology." Chapter III is an exhaustive chap-

ter on the inner morphology of the higher plants. The various cell tissues, the cell walls, and cell contents are freely shown by numerous line drawings. Pharmacists should be more familiar with this subject, and the time is coming when a microscope will be an item in the equipment of every pharmacy. Chapter IV treats of the classification of Angiosperms yielding drugs, food products, and other economic products of general interest; and Chapter V is devoted to the cultivation of medicinal plants. Much must be done in this direction in the near future.

Part II is of special interest to pharmacists. In Chapter I all of our crude drugs are carefully considered, and all allied plants are mentioned showing the points of difference. Crude drugs, microscopic sections, tissue elements, crystals, etc., are fully illustrated, and the descriptive matter carefully written, concise and complete. In these days when most drugs are bought in powdered or ground condition, the pharmacist should be able to determine the purity of his purchases. He may become able to do this by careful study of Chapter II of this section. Powdered drugs and food products are here grouped according to the cellular tissues present, the size and character of the starch granules, the various crystals, etc.

In Part III the reagents necessary for microscopic work are presented, and microscopic technic discussed. Part IV is a new section. About forty pages are included, treating of the microanalysis of the more important active constituent of drugs. This is interesting and instructive to any one familiar with the use of the petrographical microscope.

Professor Kraemer is our most thorough and painstaking investigator in this department of study, and this edition shows the exactness of detail that characterizes his work. While his technical knowledge is the highest, his writings are singularly free from burdensome technicalities, and are easily understood by the student. I have read this edition with much pleasure and am glad to give expression of my appreciation of it.

C. F. NIXON.

THE PHARMACOPŒIA AND THE PHYSICIAN. By Robert A. Hatcher, M.D., and Martin I. Wilbert, Ph.M. Third revised edition. Chicago: American Medical Association Press, 1910.

This volume consists of a series of articles which originally appeared in the *Journal of the American Medical Association*, discussing the chief substances in the United States Pharmacopœia, classifying them according to their uses and describing their methods

of combination and how they may take the place of many proprietary preparations for which extravagant claims have been made.

The book has been thoroughly revised and brought into accord with present-day teachings and facts. The authors are champions of the U. S. Pharmacopœia and the well-established remedies contained therein. The only reason for the extensive use of hundreds—yes thousands—of preparations which are upon the market to-day is simply the fact that we know very little about any of them. This work of Hatcher and Wilbert is a step in the right direction in that it acquaints the medical student and the practitioner with the nature and uses of the official substances and their preparations.

DIE ATHERISCHEN ÖLE. Von E. Gildemeister und Fr. Hoffmann. Zweite Auflage von E. Gildemeister. Bearbeitet im Auftrage der Firma Schimmel & Co. in Miltitz bei Leipzig. Erster Band. Mit zwei Karten und Zahlreichen Abbildungen. Verlag von Schimmel & Co., Miltitz bei Leipzig. (Für den Buchhandel: L. Staackmann, Leipzig), 1910.

It is now a little more than ten years since the first edition of the work on "The Ethereal Oils," by Gildemeister and Hoffmann, was published by Schimmel & Co. This book has been invaluable to the student of phytochemistry as well as the dealer and analyst of volatile oils. During this time so many investigations have been carried on and the literature has been so enriched, that we are indeed fortunate in having a new edition comprising these advances. The amount of material gotten together by Dr. Gildemeister was so large that it has seemed advisable to the firm of Schimmel & Co. to publish the work in two volumes. The first volume, which has been received, includes the historical facts concerning the individual oils and remains much the same as originally written by that master of historical studies, Dr. Fred. Hoffmann. This volume also contains a description of the principle constituents of the volatile oils and the assay methods used in determining them. A new feature is the chapter on the method for extracting the odorous principles from flowers, through extraction, enfleurage, and maceration. The chapter on "the theoretical principles involved in the distillation of ethereal oils and the separation of the various constituents through this process" has been omitted from this volume and been made into a distinct volume as already noted in this JOURNAL (July, p. 345).

The well-known tables of the first volume have been revised

and enlarged and an additional table is given which will be found of great value to the analyst. By using 1.5 Gm. of the volatile oil and adding the required amount of half-normal potassium hydroxide solution for saponification, not only can the ester value of the oil be determined, but the per cent. of the esters and alcohols may be ascertained without any further calculation. This promises to be of the greatest possible assistance to all those who desire an accurate knowledge of the character of the oils that they purchase.

The subject matter has been well prepared; the necessary facts with citation to literature have been given, and the information includes not only the recent scientific researches regarding the principle constituents of the volatile oils and their constitution, but the approved laboratory methods for obtaining a true knowledge of the quality of the respective oils under consideration. Every dealer in volatile oils and especially all retail pharmacists will find this book of great interest and practical value.

E. MERCK'S ANNUAL REPORT OF RECENT ADVANCES IN PHARMACEUTICAL CHEMISTRY AND THERAPEUTICS. 1909. Volume xxiii. E. Merck, Chemical Works, Darmstadt. 1910.

In addition to the comprehensive review of recent literature relating to pharmaceutical products and therapeutics there is an excellent chapter of 84 pages on "Serum Therapy and Bacteriotherapeutic Preparations." We do not recall having seen anything so complete and instructive and yet concise. Among the most interesting reports, from a therapeutic viewpoint, is that on the use of perhydrol for combating nasopharyngeal and oral infections. Dr. Simon Flexner, of the Rockefeller Institute for Medical Research, recently pointed out that the virus of poliomyelitis can enter the nervous system through the abraded mucous membrane of the nose, and that the virus is quickly destroyed by a dilution of perhydrol. It is similarly used in summer catarrh and scarlet fever.

A TREATISE ON PHARMACY FOR STUDENTS AND PHARMACISTS. By Professor Charles Caspari, Jr., University of Maryland. Fourth edition, enlarged and revised. Illustrated with 330 engravings. Philadelphia and New York: Lea and Febiger, 1910.

The object of this text-book is to furnish the student with the *raison d'être* for the processes and tests employed in the preparation and testing of pharmaceutical products; and to give the retail pharmacist a trustworthy guide for use in conjunction with the U. S. Pharmacopœia and National Formulary. It is not too much to say



that it amply fulfils this purpose and is an excellent companion to these standard works.

The work is divided into three parts. Part I comprises General Pharmacy, which includes the general study of pharmaceutical processes, weights and measures, etc. Part II is devoted to Practical Pharmacy and treats of the official galenical preparations, together with many of the operations conducted at the dispensing-counter. In Part III we find an excellent treatment of Pharmaceutical Chemistry.

All parts of the book are well handled and display the author's ability as a writer, his excellent judgment as a scholar and judicious reader, and his competence as a practical writer and analyst of many years' experience. The book will appeal to students in pharmacy, the retail pharmacist, and the manufacturer.

PLANT ANATOMY FROM THE STANDPOINT OF THE DEVELOPMENT AND FUNCTIONS OF THE TISSUES AND HAND-BOOK OF MICRO-TECHNIC. By Prof. William Chase Stevens, University of Kansas. Second edition, revised and enlarged. With 152 illustrations. Philadelphia: P. Blakiston's Son & Co., 1012 Walnut Street, 1910. \$2.00 net.

This book of Stevens has a number of features to commend it. The "generalized diagrams" used throughout the book enable the student to grasp almost immediately the three views of cells and tissues. This is especially important to the pharmacognosist in his study of powdered drugs and foods.

In the present edition Prof. Stevens has added a chapter on reproduction, and considers the processes of nuclear division, behavior of pedigree hybrids, the working of Mendel's laws, and theory of pangeneic interchange. These discussions are of importance even to the pharmacist, as sooner or later our studies on drugs must begin with the growing plants. Furthermore, it is quite likely that the breeding of drug plants will furnish data of the greatest value for the study of the valuation of crude drugs. A sufficient number of experiments have already been made upon species of *Cinchona* and varieties of *Atropa Belladonna* to show not only the "mosaic character of the offspring of hybrids" but that there is a variation in the active constituents.

The point of view of the author of this text-book is a good one and the book is to be recommended to both teachers and students of our schools and colleges of pharmacy.

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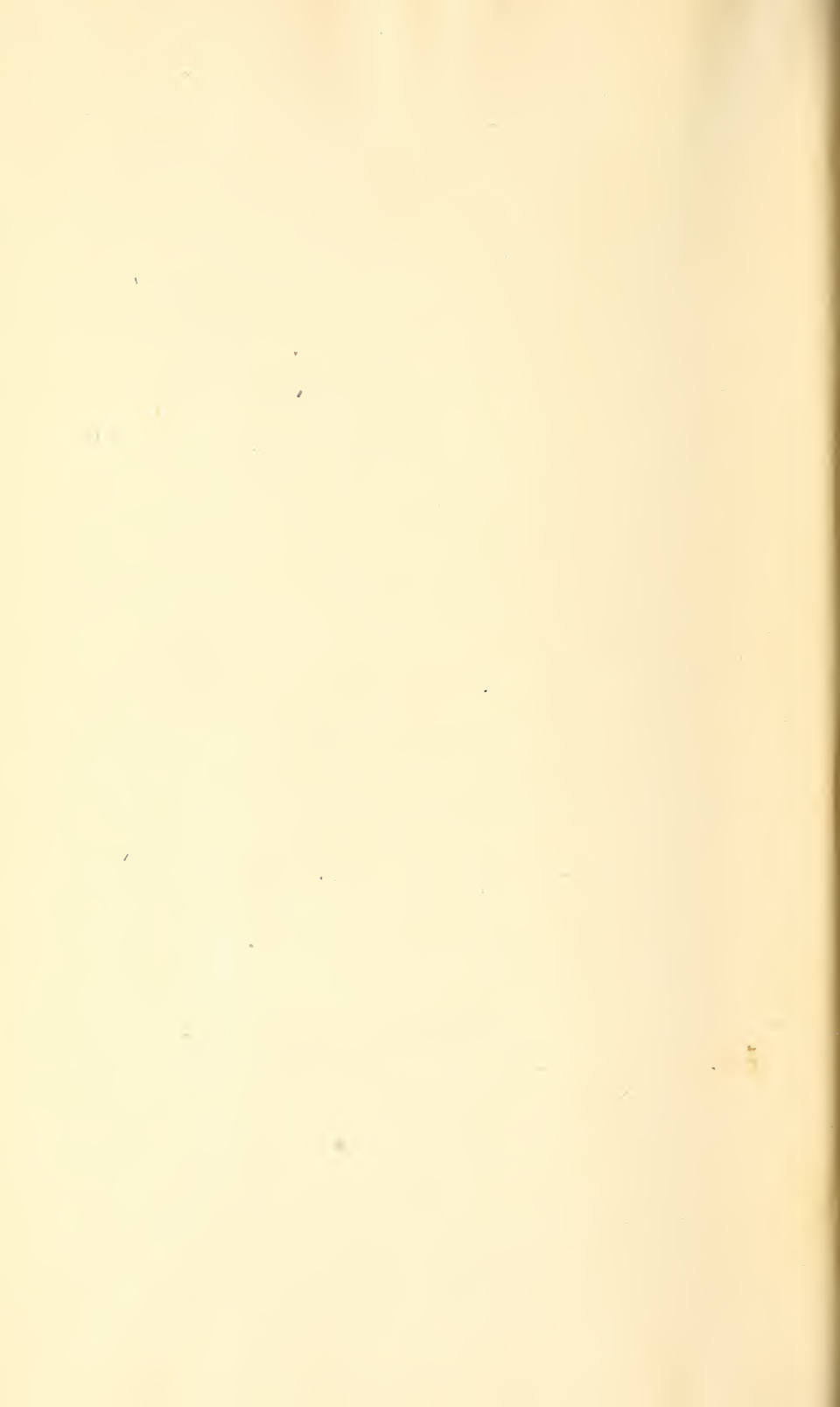
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